ournal

of the AMERICAN PHARMACEUTICAL ASSOCIATION

DECEMBER
1959

Practical Pharmacy Edition

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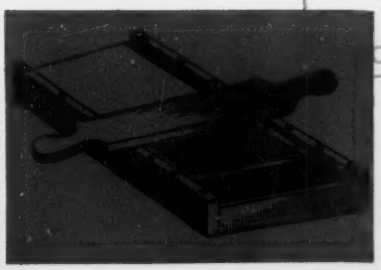
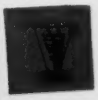
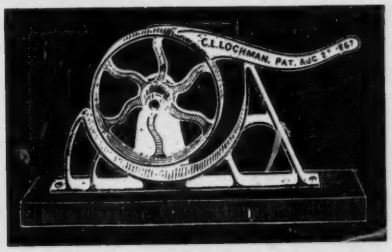
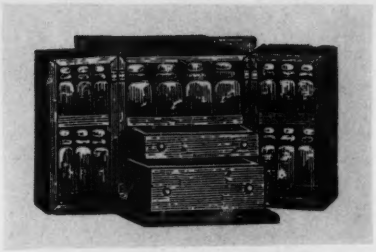


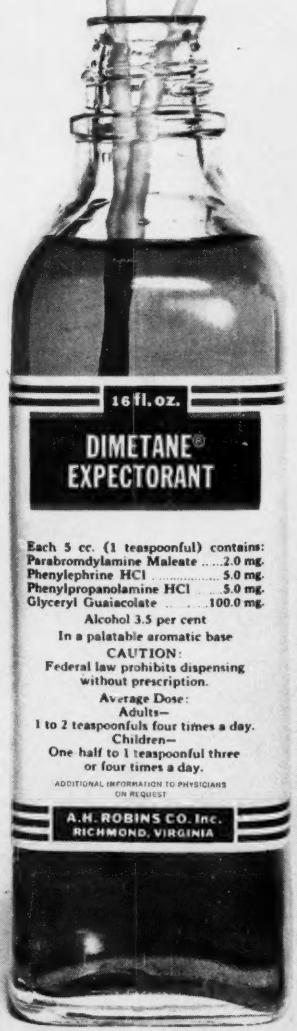


Season's Greetings





for cough



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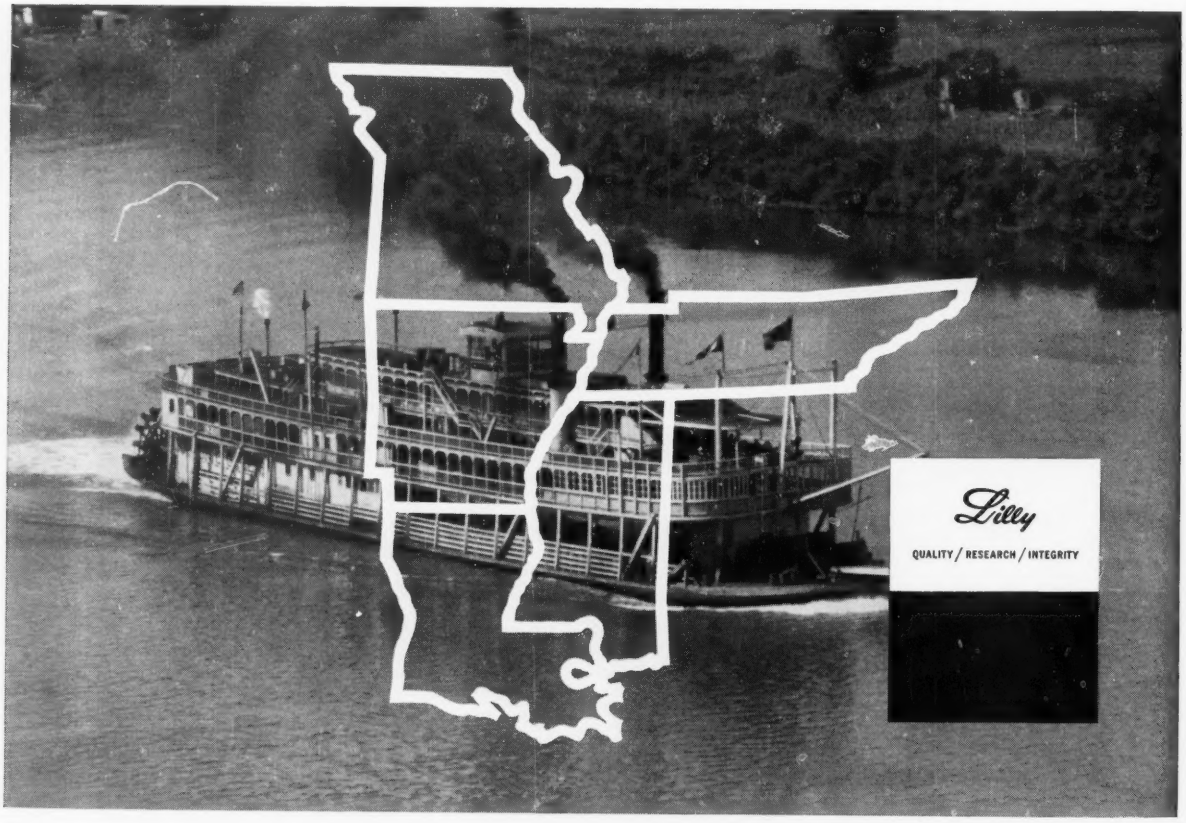

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Journal
of the **AMERICAN PHARMACEUTICAL ASSOCIATION**

Practical Pharmacy Edition

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This Journal is the official monthly publication of the AMERICAN PHARMACEUTICAL ASSOCIATION, dedicated to the elevation and unification of the profession of Pharmacy through communication of authoritative scientific professional, and cultural information. It is devoted to the education of pharmaceutical practitioners, and it functions as the professional voice of Pharmacy, which is directed to all members of the profession of Pharmacy in education, government, industry, and professional practice.

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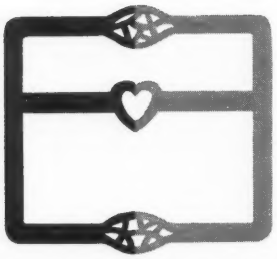

FOR GREATER LATITUDE IN SOLVING THE PROBLEM HYPERTENSION WITHOUT SIGNIFICANT POTASSIUM DEPLETION

NEW RAUTRAX

RAUTRAX, a combination of Raudixin with Ademol (flumethiazide)—**the new, safe nonmercurial diuretic**—controls all degrees of hypertension. Elimination of excess extracellular sodium and water is rapid and safe.[1-5] Potassium loss is less than with other nonmercurial diuretics;[1-3] and, in addition, Rautrax increases protection against potassium and chloride depletion during long-term management by including supplemental potassium chloride.

The dependable diuretic action of Ademol rapidly controls the clinical and subclinical edema often associated with cardiovascular disease. And after Rautrax has normalized the fluid balance, the normal serum electrolyte pattern is not altered appreciably by continued administration.[4] Ademol also potentiates the antihypertensive action of Raudixin.[1] In this way a lower dose of each component controls hypertension effectively and safely . . . with fewer side effects.

REFERENCES: 1. Montero, A. C.; Rochelle, J. B., III, and Ford, R. V.: New England J. Med 260:872 (April 23) 1959. 2. Fuchs, M.; Bodi, T., and Moyer, J. H.: Am J. Cardiol 3:676 (May) 1959. 3. Fuchs, M., and others: Monographs on Therapy 4:43 (April) 1959. 4. Montero, A. C.; Rochelle, J. B., III, and Ford, R. V.: Am. Heart J 57:484 (April) 1959. 5. Rochelle, J. B., III; Montero, A. C., and Ford, R. V.: Antibiotic Med. & Clin. Ther. 6:267 (May) 1959. LITERATURE AVAILABLE ON REQUEST

SQUIBB

Squibb Quality—
the Priceless Ingredient

RAUDIXIN (Squibb standardized whole root Rauwolfia Serpentina) / ADEMOL (Squibb Flumethiazide) / POTASSIUM CHLORIDE

'RAUDIXIN' ®, 'RAUTRAX' AND 'ADEMOL' ARE SQUIBB TRADEMARKS

HEW to seek legislation curbing illegal sale of amphetamine—During the same press conference at which Health, Education, and Welfare Secretary Arthur S. Flemming warned against the use of cranberries which had been contaminated with aminotriazole, Secretary Flemming disclosed that he intended to ask Congress for legislation to curb the illegal sale of amphetamine. The legislative recommendations under consideration by the HEW secretary include a requirement that manufacturers, wholesalers and retailers be registered, that they be subject to federal inspection and that they keep records of all amphetamine sales. Asked if the proposed legislation was in any way similar to the Boggs Bill which has not passed in previous sessions of Congress, Flemming replied that there may be some similarity. He was not certain whether HEW recommendations would include the regulation of barbiturates as well.

False advertising of dentifrices concerns surgeon general—Surgeon General Leroy E. Burney of the Public Health Service agrees with the American Dental Association in that false advertising of dentrifrices is of considerable public health concern. The Surgeon General points out that while dentrifrices are necessary for care of the teeth, they are primarily aids for cleaning them. No dentrifrice in itself can prevent tooth decay or pyorrhea or any other disease, and no dentifrice can lighten the color of teeth. In fact, Dr. Burney emphasizes, tooth "bleaches" are unsafe to use.

Carter's little pills now "liverless"—A Federal Trade Commission order barring the use of the word "Liver" in "Carter's Little Liver Pills" was upheld by the U.S. Supreme Court. The high tribunal refused to review the FTC order, which also prohibits Carter from advertising that its product increases bile flow. FTC says the product has no therapeutic value in the treatment of any disorder of the liver.

Kefauver hearings—By the time you receive this issue, the Kefauver Senate antimonopoly subcommittee will have begun their much publicized drug price hearings in Washington, D.C. Slated as witnesses the first week are Francis C. Brown, chairman and president, Schering Corporation, who will testify first on Monday, December 7; representatives of the Arthritis and Rheumatism Foundation; J.T. Connor, president, Merck and Company, Inc.; Dr. Ethel Andrus, president of the American Association of Retired Persons, and Seymour Blackman, secretary and treasurer of Premo Pharmaceutical Laboratories, Inc. E.G. Upjohn, president, Upjohn Company, is scheduled to take the stand December 14. This JOURNAL will report on the progress of these hearings in the January issue.

Pharmacy Today

Student Branches

Albany College of Pharmacy—*Richard Doyle* is the new president of the APhA student branch at Union University. Working with him for the school year are *Mary Lou Schipp*, vice president; *Lois Cassidy*, secretary; and *Sue Nicholson*, treasurer.

Butler University—*Dr. Philip Boyer*, director of clinical research at Pitman-Moore Company, spoke on the use of dietary supplements in the treatment of atherosclerosis at the regular business meeting of the APhA student branch on October 16. *William Schaffer* reported on APhA's Cincinnati convention.

Duquesne University—Fair trade was the topic for a forum sponsored by the APhA student branch on October 29. Taking the affirmative side were *Max L. Miller*, secretary-treasurer of the Pennsylvania Pharmaceutical Association, and *David A. Boyd*, executive secretary of the Allegheny County Pharmaceutical Association. On the negative side were *Dr. Arthur Sharron*, instructor in Duquesne's department of economics, and *James Cawley*, graduate student in the school of business administration. Moderator was *Patty Potesta*.

Fordham University—*Jack Cooper*, director of pharmaceutical research and development division of Ciba, Inc., addressed a special meeting of the APhA student branch on October 27 on the "Stability of Pharmaceutical Preparations."

At the regular meeting of the group on October 13, the freshman class joined branch members to see the film, "Today with the Upjohn Company," in which all phases of production were portrayed.

Howard University—Talks by *Dean Chauncey I. Cooper* and faculty advisor, *Dr. Theodore Zalucky*, headlined the opening meeting of the student branch during National Pharmacy Week. In charge of the session were the new officers *Herbert L. Hunter*, president; *A. Luis LeBron*, vice president, and *Ida M. Martin*, secretary-treasurer. President Hunter welcomed the freshman class as new members of APhA and reported on APhA's Cincinnati convention while vice president LeBron outlined the significance, history and progress of National Pharmacy Week.

Loyola University—A trip to E.R. Squibb and Son and Pfizer Laboratories for January, 1960 was planned at the October meeting of the APhA student branch. In observance of National Pharmacy Week the group built two displays—one in the college of pharmacy and the other in the library. On October 22 student branches took an evening off for their annual weiner roast.

Massachusetts College of Pharmacy—The APhA Life Insurance Program was explained by *George S. Yeaton*, special agent for Minnesota Mutual Life Insurance Company at the regular business meeting of the student branch on October 6. Winner of the medical dictionary given at the end of the meeting was *Barry Norton*.

Medical College of Virginia—*William R. Maynard*, pharmacist for the division of chemistry and foods at the Department of Agriculture and Immigration in Virginia, was guest speaker at the APhA student branch's first meeting of the school year. A membership drive brought in 100 new members during September. A special pamphlet outlining the importance of APhA activities and providing a roster of the faculty and section officers was given each freshman.

Montana State University—Plans for decorating a float for the Homecoming parade and a discussion about a Christmas party and dance were the chief topics of interest at the APhA student branch meeting on October 28. *Judy Black* was chosen corresponding secretary and following the meeting a film, "Frontiers in Research," was shown. *Carl Lenzendorfer* of Billings was slated to speak at the November meeting.

New England College of Pharmacy—*Thomas A. Brady*, president of the Massachusetts Pharmaceutical Association, spoke on National Pharmacy Week to 200 members of the APhA student branch on October 9. He outlined the inception of pharmacy week 35 years ago, and stressed the importance of membership in pharmaceutical associations.

Northeast Louisiana State College—*Dr. James Wade*, cardiac and internal medicine specialist, at a meeting of the APhA student branch on October 20, explained the technics of cardiac catherization and described cardiac drugs in use today.

Ohio Northern University—*Llyn Lloyd*, *Mel Deutsch*, *Fred Pusser* and *Leroy Weaver* have been appointed to review and revise the constitution of the APhA student branch. *Llyn Lloyd*, who attended the APhA Cincinnati convention as a delegate of ONU was elected alternate delegate for 1960 for student pharmacy sections.

Philadelphia College of Pharmacy and Science—Heading the APhA student branch this year are *Keith Weikel*, president; *David Lutz*, vice president; *Betty Ann Mason*, secretary, and *Maven Myers*, treasurer. *Dr. John C. Young* has been named faculty advisor.

Dr. William S. Apple, secretary of APhA (seated center) describes the modern functions of a professional society as (left to right) Dr. E. O. Lange of Ciba Ltd., Basle, Switzerland, Goodsell F. Waters, president of the APhA Northern New Jersey Branch, Paul Gavaris, president of Rutgers student branch and Jack Cooper of Ciba Pharmaceuticals Inc., Summit, New Jersey look on. Dr. Apple discussed the role of APhA in pharmacy today and Cooper detailed "The Objectives of Industrial Pharmacists in APhA" at a joint meeting of the student and NNJ branches on October 7

Purdue University—*Robert Hoey*, salesman for West Bend Drug Company, described "The Place of the Wholesaler in the Drug Field" to APhA student branch on October 8. Elections put *Gerald Taylor* at the helm as president, *Douglas Driscoll* as vice president, *Alice Nelson* as secretary and *Mary Losey* as treasurer.

University of Arizona—Emphasizing the importance of research and the ability of the research worker to follow the line to which his research leads, *Dr. Gustavson*, retired professor of chemistry, spoke to members of the APhA student branch at their October meeting. His title—"Follow the Rabbit." *Dr. Joseph Zapotocky*, faculty advisor, presented "Scripts," the pharmacy wives' club, with its charter which *Mrs. Elvern Orr*, president, accepted.

University of Buffalo—*Dr. George F. Archambault*, chief, pharmacy branch, division of hospitals, USPH, outlined careers in pharmacy with special emphasis on hospital pharmacy and the U.S. Health Service for members of the student branch of the University of Buffalo when he spoke before the group on October 20.

University of Colorado—At a combined meeting and coffee hour on September 29, *Wilson Chase*, president of the APhA student branch, spoke on the advantages of membership and *Dr. Francis C. Hammerness*, faculty advisor, discussed APhA's life insurance program. On October 18 the group held its annual picnic with members of the Colorado State Board and officers of the Colorado Pharmacal convention as special guests.

University of Georgia—The need for a pharmacist to be active in community affairs was emphasized by *Harold Hodgson*, registered pharmacist and owner of Watson's Drugs in Athens, when he spoke at a special National Pharmacy Week meeting of the APhA student branch. At the business session of the meeting, *Frank Randolph* and *George Maloney* were elected to represent the student branch at the Athens Pharmaceutical Association's meetings.

University of Illinois—A picture of pharmacy in California from the business side and the state board side was drawn for members of the student branch on October 28 by *Martin M. Rosner* and *Dr. Frederick Siegel*, faculty members.

University of Iowa—*Dean Louis Zopf* of the college of pharmacy, in welcoming new students at the October meeting of the student branch, pointed out the challenges, opportunities and

Holding the reins for the APhA student branch at North Dakota State College are (left to right) R. E. O'Neill, Jr., faculty adviser; Francis F. Bures, vice president; Vernon A. Schanilec, president; Marvin R. Moen, treasurer, Dee Ann Nelson, secretary, and Tom Hansman, membership chairman.

responsibilities pharmacy offers to students. He also awarded scholarships and prizes earned by students during the preceding year. In addition *Jack Cohen*, president of Rho Chi, and *Emilie Blume*, president of Kappa Epsilon, awarded prizes for their respective fraternities.

University of Kansas—Taking charge of the APhA student branch this year are the officers elected last spring. *Robert C. Iott* is president, *Larry Stark*, vice president, *Mrs. Judith L. Hearn*, secretary, and *Deanne Crouse*, treasurer.

University of Kansas City—*Fred L. Fellers*, president, *John Schultz*, vice president, *Joyce Banken*, secretary, and *Tom Todd*, treasurer are handling affairs for the APhA student branch from the officers' bench this year.

University of Kentucky—*Dr. Howard Hopkins*, new head of the pharmacy department at Kentucky College of Pharmacy is faculty advisor to the APhA student branch.

University of Maryland—"Narcotics, Narcotic Laws and Their Relationship to Pharmacy" was the topic discussed by *Mrs. Baldwin*, assistant to the supervisor of the Bureau of Narcotics, at a special meeting of the APhA student branch on October 20. She emphasized particularly the pharmacist's duty in regard to narcotics and the results of dope addiction.

University of New Mexico—*Ronald Paynter* has taken over the post of president of the APhA student branch of the University of New Mexico. Serving with him are *Johnny Volpato*, vice president; *Shirley Hollandsworth*, secretary; *Dr. Marvin Malone*, treasurer and faculty advisor; *John Lee*, student senator; *Richard Paine*, alternate student senator; *Lyle Raker*, historian-corresponding secretary; *Jesse Smith*, social chairman, and *Elbert Clemmet*, program chairman.

University of Pittsburgh—Balloting results at the APhA student branch reveal *R. Lee Pfrogner* as president, *Stanley Marks* as vice president, *Burton Bogden* as secretary and *Thomas Rouse* as treasurer.

University of Puerto Rico—*Blas Anaya* was elected president of the APhA student branch; *Hilda Garcia Rivera*, vice president; *Ivette Martinez Ramirez*, treasurer; *Heidy Ramirez*, secretary, and *Nilda Gandulla* and *Ivelisse Lebron*, vocals. The counselor is *Dr. Leo B. Lathroum*.

University of Wisconsin—Using films—one on the action on the heart valves and one on fire hazards in the use of flammable anesthetics—to bring out his points, *Dr. Joseph G. Cannon*, faculty adviser, discussed the use of movies in the health field with members of the student branch on October

David J. Irvine (left), past president of the APhA Puget Sound Branch, was honored at the annual meeting of the group in October. For his outstanding work in professional organizations, he was presented with a bronze plaque, the group's 1959 merit award, by J.E. Birmingham (right), the outgoing president.

Presenting apothecary jars to (*left to right*) John A. Lynch, assistant professor of pharmacy administration at Temple University school of pharmacy, and John Kramer, registrar at the Philadelphia College of Pharmacy and Science, is Mrs. Abram P. Karsh. The jars represented a collection of pharmaceutical antiques, valued at $3,500 and willed to the schools by the late Abram P. Karsh who died in April, 1959. Karsh, a graduate of the Philadelphia College of Pharmacy and Science, had been the owner of the 100-year old Colonial Drugstore in Philadelphia.

Washington State University—*Gary Bergstrom*, new president of the APhA student branch, appointed committees to set up a booth in the activities roundup, organize the "Pharmacy Mix" and prepare for the Pharmic-Vet basketball game. *Ronald Swanson* is vice president and *Beverly Holmes* secretary for the school year.

Local Branches

Chicago Branch—*E.J. Carroll*, director, economic research, Merck, Sharp and Dohme Division, Merck and Company spoke on various prepaid prescription insurance plans and their effect on pharmaceutical practices" at a dinner meeting of the APhA Chicago branch November 4.

Indianapolis—Stressing the specificity in antibiotic therapy, *Dr. Roy A. Behnke*, chief of medical service, Veterans Hospital, discussed the use and abuse of antibiotics before members of the APhA Indianapolis branch on October 21. Also in the spotlight that evening were a report by *Paul Delbauve* outlining future meetings and an outline of pharmacy week activities by *Dr. Karl Kaufman*.

Memphis—"You and Your Profession" will be the topic on which *Burns Geiger* of Pfizer Laboratories will speak at the installation banquet for the APhA student branch in December. The announcement of his selection as speaker was made at the October meeting of the group at which *Dr. F. H. Knox, Jr.*, chief of cardiology, Kennedy Veterans Hospital, spoke.

Northern California—An illustrated lecture on plastic and reconstructive surgery highlighted the October meeting of the APhA Northern California branch. *Dr. George W. Pierce* was the guest speaker. At the board of directors meeting the group voted to assist the University of California in sponsoring an exchange student from Turkey and decided to co-operate with the career day programs of Bay Area high schools.

Northern New Jersey Branch—*Goodsell F. Waters* has been elected president of the APhA Northern New Jersey Branch. Swept into office with him were *William Fink*, *Mrs. Florence S. Frick*, vice presidents; *Michael Iannarone*, secretary-treasurer, and *Dr. John L. Voigt*, publicity chairman.

For the third year Pacific Drug Distributors gave a full-year tuition scholarship to the University of Southern California's school of pharmacy. Ronald D. Holt, director and general manager of Pacific Drug (far right) presented the check for $950 to Dr. Alvah G. Hall (far left), pharmacy dean. Sheldon Warren and John F. Frey (center) shared in this year's grant.

Associations

Allegheny County Pharmaceutical Association—ACPhA's active participation in the Pittsburgh bicentennial program won for the association a science award plaque from the Pittsburgh Bicentennial Association. *Ed Schaughency*, KDKA radio and television announcer presented the plaque at the dinner-dance which concluded the celebration.

American Association for the Advancement of Science—Routine business matters occupied the attention of the AAAS board of directors at its meeting in Washington, D.C., October 3 and 4. Discussions also involved approval of co-operation and assistance to the National Association of Science Writers in the establishment of Council for the Advancement of Science Writing.

American Association of Colleges of Pharmacy—The AACP Executive Committee meeting in Chicago, Illinois, November 9–10, selected the University of Colorado college of pharmacy in Boulder, Colorado as host for the 1960 AACP annual meeting. Dates for the meeting, which will be held jointly with a general seminar, are July 3–9. A seminar committee is being appointed, and is scheduled to meet in Boulder in January to arrange for the meeting. Another action of AACP executive committee was the selection of *Dr. Charles Boyd Granberg*, professor of pharmacy at Drake University college of pharmacy, Des Moines, Iowa, to become editor of the *American Journal of Pharmaceutical Education*, effective January 1, 1961.

American Association of Colleges of Pharmacy and National Association of Boards of Pharmacy, District 2—Elected chairman at the annual conference of boards and colleges of pharmacy (November 22–24) was *Dean Albert J. Sica* of Fordham University, college of pharmacy. He has served as chairman of the time and place committee at the 1959 conference.

American Dental Association—*Dr. Harold Hillenbrand*, secretary of ADA, announced last month the appoint-

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sense

Vernon O. Trygstad, director of pharmacy service, Veterans Administration, received the first annual Andrew Craigie Award at the 66th annual convention of the Association of Military Surgeons of the U.S. in Washington. Dr. Benjamin Carey (right), medical director of Lederle Laboratories, presented the award, established by his firm in recognition of outstanding accomplishment in the advancement of professional pharmacy within the federal government. Trygstad, president of the American Society of Hospital Pharmacists, was selected by an AMS honors committee. Watching the presentation is Maj. Gen. H.H. Twitchell (left), U.S. Air Force and AMS president. The award honors the memory of the first Apothecary General of U.S. military forces.

ment of *Dr. Leland C. Hendershot* and *Dr. John J. Hefferren* to the staff of the Council on Dental Therapeutics. Dr. Hendershot, formerly a pharmacologist with Dow Chemical Company, will be assistant secretary of the council and Dr. Hefferren, formerly a chemist with AMA director of the division of chemistry.

National Tuberculosis Association—Released on November 5 was the 1959 annual report of NTA which pictures in a 32-page booklet the complex and varied problems of tuberculosis control. The well-illustrated report uses as its title, "3-Point Attack on TB! —detection, treatment, research."

Nebraska Pharmaceutical Association—On a whirlwind tour of Nebraska recently went *Carl K. Raiser*, assistant to the president of Smith Kline and French Laboratories. The tour to address joint meetings of physicians and pharmacists was arranged by NPhA. Talks were given at Scottsbluff, Lincoln and Omaha and stressed the need for co-operation of all members of the health team.

Pharmaceutical Manufacturers Association—Production and foreign operations, marketing and medical and scientific developments, and socio-economic problems will key the eastern regional meeting of PMA December 7–9. The annual award dinner scheduled for December 8 will honor *Dr. Cyril N.H. Long*, eminent endocrinologist and physiologist, of Yale University medical school.

Society of Pharmacists in Industry—Guest speaker at the November meeting of the Society of Pharmacists in Industry was *Louis E. Kazin*, editor of *Drug Topics*.

Rho Chi Society—*Dr. Lloyd M. Parks*, dean of Ohio State University's college of pharmacy, was elected national president of Rho Chi in a mail ballot election in November. He will be installed at the close of the 1960 convention to serve a term of two years.

Colleges

Brooklyn College of Pharmacy—The Research Institute of Long Island University's Brooklyn college of pharmacy has received two grants—one from the National Institutes of Health and the other from Carter Products, Inc. The NIH grant was awarded to *Dr. Shirley D. Kraus*, associate professor of pharmacology, for the study of steroid hormone-like action of glycyrrhetinic acid. *Dr. James W. Ingalls*, associate professor of pharmacology, received the Carter grant for studies in experimental heart disease. Honored at a dinner-dance on November 8 was *Dr. Arthur G. Zupko*, dean of the 69-year-old college. The alumni association paid tribute to him as he began his fifth year as dean.

Rutgers University—The college of pharmacy has received an oil portrait of the late *Dr. Philemon E. Hommell*, a founder and first dean of the New Jersey State University college from *Jean L.A. Hommell*, of Perth Amboy, New Jersey, Dr. Hommell's brother who painted the picture. It will be hung in the dean's office.

St. John's University—The latter part of October provided three opportunities for pharmacy students to hear outstanding speakers. *James Beeny, Jr.* of the Ames Company spoke to senior students on diagnostic aids with the aid of a sound film and demonstrations; *Dr. Gilman N. Cyr*, head of the pharmaceutical formulation department of Squibb Institute for Medical Research, as guest speaker at the October 23 meeting of the Beta Delta Chapter of Rho Chi Society, discussed pharmeaceutical research and the development of drug products; *Frank Erranto*, district manager of the Burroughs Wellcome Company, Inc. described the field of medical detailing to senior students on October 28.

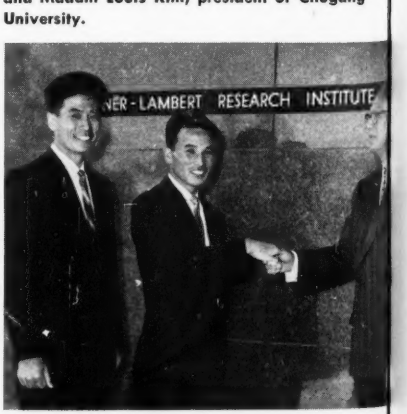
Wayne State University—Guest speaker at a recent honors convocation at Wayne's College of Pharmacy was *Lloyd Beemer*, manager of sales training at Parke, Davis and Company. His topic—the importance of effective salesmanship in pharmacy. Two awards for $100 were made to *Stephen Dworziann* (Maicki Award) and to *Martin Peltz* (Rho Pi Phi Award).

University of Arkansas—Pulaski County pharmacists were guests of Arkansas' school of pharmacy on October 22 for a special program on seminars and conferences. A faculty panel discussed ways and means of providing "post-graduate" instruction for pharmacists and an open forum centered around topics of interest for seminars.

University of Georgia—Representatives of 14 Georgia colleges attended the third Annual Pre-Pharmacy Advisors' Conference on October 2–3 at the University of Georgia Center for Continuing Education. *Professor Charles L. Baucher* chairmanned the event which brought nine drug manufacturers, three retail pharmacists and three hospital pharmacists together to outline the opportunities awaiting the pharmacy graduate.

A book dedication dinner honored *Dr. Robert C. Wilson*, dean emeritus of the school of pharmacy, on November 24. That was the date his book, *Drugs and Pharmacy in the Life of*

Elmer H. Bobst, chairman of the board of Warner - Lambert Pharmaceutical Company, greeted (left to right) Il Hyuk Kim and Dong Hun Sohn, teachers in the pharmacy college of Chugang University in Seoul, Korea. The Koreans began a year of post-graduate work in research and manufacturing pharmacy at the Warner-Lambert Research Institute. The post-graduate tour was arranged by Bobst, who was instrumental in establishing the pharmacy school in Korea Co-operating with him were the American-Korean Foundation and Madam Louis Kim, president of Chugang University.



Fullfilling One's Obligations

Edwin M. Holt is one person who will never abandon his obligations and responsibilities as a pharmacist and as a member of the AMERICAN PHARMACEUTICAL ASSOCIATION.

Even though Dr. Holt will be 85 years old next January 13, and is restricted to life in a hospital sanitarium, he has contributed to the APhA Building Fund. When he presented the check to Dr. William S. Apple, secretary and general manager of the APhA, last October 27, he explained that "my earning power days are gone, and I can hardly see to write, but on the theory that every little bit helps, I am contributing five dollars for the building fund."

Dr. Holt, a native of North Carolina, received his Doctor of Pharmacy degree from the Philadelphia College of Pharmacy in 1899, and he joined the U.S. Public Health Service as a pharmacist in 1900. He served with distinction for 39 years in numerous stations throughout the country. Dr. Holt joined APhA in 1927, and became a Life Member in 1946. He retired from active service to his profession in 1939 and has been in the Waverly Sanitarium in Rockville, Maryland since 1956.

To you Dr. Holt, for your recognition of a responsibility each of us should have, we give our grateful appreciation in the simple word "thanks."

Georgia, was released. Sponsored by the University of Georgia School of Pharmacy Alumni Society, the dinner was held at the University's Center for Continuing Education.

University of Michigan—The annual "Pharmacy Lectures" for practitioners and the second "Pharmacy Day" for career-minded Michigan high school students were held in October at the college of pharmacy in Ann Arbor. Activities for "Pharmacy Day" on October 24 included tours, laboratory demonstrations, special exhibits and discussions of pharmacy careers.

Government

Department of Agriculture—Retiring at the end of October was *Dr. John J. Willaman* of the agricultural research service's eastern utilization research and development division in Wyndmoor, Pennsylvania. Dr. Willaman formerly worked at the Rohm and Haas Company and developed enzymes from bacteria and molds that are still in wide commercial use. He has had charge at the Wyndmoor Laboratories of the screening process of plants in search for steroids.

U.S. Atomic Energy Commission—*Dr. Nathan H. Woodruff* has been appointed as director of AEC's recently established office of health and safety. At the same time, *Dr. Forrest Western*, who was designated acting director of the office when it was established on September 15, was named deputy director. The office will develop and recommend health standards for protecting workers and the public from atomic energy induced radiation.

Industry

Chicago Pharmacal Company—*Harold F. Laycock*, formerly field sales manager for Maltbie Laboratories Division of Wallace and Tiernan, has been appointed general sales manager for Chicago Pharmacal Company. A registered pharmacist, Laycock has had a long career in the marketing, merchandising and detailing side of the pharmaceutical field.

Ciba Pharmaceutical Products—*Vincent A. Burgher*, vice president in charge of sales at Ciba, retired October 31 after 32 years with the firm. Dr. Burgher received his Doctor of Pharmacy degree from George Washington University where he served later as a faculty member. He joined Ciba in 1928 and became a vice president in 1942.

Geigy Chemical Corporation—A multimillion dollar research building for the development of future drugs was dedicated by Geigy Chemical Corporation on October 16. Three Nobel prize winners—*Dr. Paul Karrer*, professor of organic chemistry at the University of Zurich, *Dr. Paul Meuller*, a director of J.R. Geigy, and *Dr. Vincent DuVigneaud*, professor of biochemistry at Cornell University medical college—participated in the dedication ceremonies along with *Dr. Austin B. Smith*, president of the American Pharmaceutical Manufacturers Association, *Dr. Adolf Krebser*, director of research for J.R. Geigy of Basle, Switzerland, and *Charles A. Suter*, executive vice president of the American subsidiary of J.R. Geigy of Switzerland.

Hazleton Laboratories—*Dr. Ivor Cornman* has been named assistant director of research for Hazleton and *Edward A. Garlock* has been appointed research application specialist in chemistry with the firm. Dr. Cornman has been with Hazleton since 1955 and will continue to serve as chief of the department of cell biology.

Lederle Laboratories—From manager of the central sales section for Lederle *Maxwell James* has been promoted to the newly created post of trade relations manager. He is a veteran of 25 years in the pharmaceutical industry having joined Lederle in 1935. His responsibilities will include trade relations with all segments of the pharmaceutical industry.

Eli Lilly and Company—*Emory J. Walker, Jr.*, will take over as manager of the new sales district established by Lilly, with headquarters in Lubbock, Texas. Walker was graduated from the University of Houston with a BS degree in pharmacy and became a registered pharmacist in Texas.. Before joining Lilly he was associated with Mading's Drug Stores in Houston.

Vernon O. Trygstad (*left*), president of the American Society of Hospital Pharmacists, presented a copy of the *American Hospital Formulary Service* to John I. Spreckimyer (*right*), administrator of the hospital ship "S.S. Hope" which will tour the world as a part of project HOPE, a program to promote world peace through increased understanding between the U.S. and other nations.

S. E. Massengill Company—*Francis S. (Bill) Taft* stepped up into the newly created position of plant superintendent at S.E. Massengill Company recently from his post as chief chemist in the control laboratory. Taft joined Massengill after his graduation from the University of Michigan.

McNeil Laboratories, Inc.—At a meeting of the board of directors of McNeil Laboratories, *Robert E. Johnston* was elected treasurer. He is a graduate of Drexel Institute of Technology and has been assistant to the treasurer since 1958. Before joining McNeil, Johnston was senior accountant with Scovell Wellington and Company.

Mead Johnson and Company—Three major promotions in the research division find *Dr. James M. Tuholski* moving into the post of director of product development, *Dr. George W. Brown* taking over Dr. Tuholski's vacated spot of clinical research director and *Dr. Richard T. Arnold* accepting the newly created position of director of research.

E.P. Anderson, executive vice president of Vick Chemical Company, receives the silver "Oscar-of-industry" trophy for Vick's annual report, judged best in the board consumer category in the 19th annual report survey by *Financial World*. Dean Joseph Taggart of the graduate school of business administration at New York University presented the award, the first to be made to a drug company since 1956, at the annual awards banquet on October 25. Vick's report also won the bronze "Oscar" for the best in the pharmaceutical industry.

Purdue Frederick Company—*Captain Richard L. Whittaker*, USAF (MC), received the annual Purdue Frederick Air Force Medicine Award at the graduation exercises of the Gunter branch, School of Aviation Medicine. The second air force medicine student to be given the plaque and mess dress uniform, Whittaker was selected for his outstanding leadership, military attributes and scholastic record.

A. H. Robins Company—*Robert J. Elkin* has been appointed to the newly created position of marketing research director. Elkin received his BS degree in pharmacy in 1952 from the University of Connecticut college of pharmacy and his MS in business administration in 1958 from Rutgers University.

Rowell Laboratories, Inc.—*Dr. Ben E. Greenwell* has joined the staff at Rowell as research director. A graduate of Monmouth College, he received his PhD from the University of Illinois. He moves to his new post from Abbott Laboratories where he has been in research for nine years.

Schering Corporation—New director of public relations for Schering is *Raymond F. Fagan*. He joined the firm as an analyst in the management research department in 1954 and had been a member of the company's public relations department since 1955.

Searle Chemicals, Inc.—On November 1 the New York offices of Searle Chemicals was moved to Chicago to the headquarters of G.D. Searle and Company, the parent company. *Robert H. Snyder*, vice president of Searle Chemicals, became general manager in addition to his other duties.

Schieffelin and Company—*Lloyd C. Bender* is the new sales manager of the pharmaceutical laboratories division of Schieffelin and Company. His background includes many years of experience in the pharmaceutical field in sales supervision and training with E.L. Patch Company and Armour Laboratories. He comes to Schieffelin from the Sherman Laboratories of Detroit.

Smith Kline and French—*Dr. Joseph V. Swintosky* has been promoted to the post of principal research pharmacist at SKF. He has been serving as group leader in the pharmaceutical research section. After receiving his PhD from the University of Wisconsin in 1948, Dr. Swintosky remained there as assistant professor of pharmacy until 1953 when he joined SKF as senior scientist.

Wallerstein Company—*Ervin Rogers, Jr.* is the new director of sales training for Wallerstein. Before joining Wallerstein, a division of Baxter Laboratories, Inc., he was associated with the Armour Pharmaceutical Company.

Pharmacists

Julius M. Amberson, Captain, MC US Navy (Ret), was cited by the Bureau of Medicine and Surgery of the U.S. Navy for "exceptional service during the last 30 years." Dr. Amberson is associated with the medical department of the Norwich Pharmacal Company as director of medical research. The commendation was presented to him at a special ceremony by Vice Admiral Thomas Coombs, commander Eastern Sea Frontier and commandant third naval district.

Edward C. White of Hoboken, president of the New Jersey Pharmaceutical Association and owner of one of the state's oldest pharmacies, took the stump for higher education during the recent election campaign in New Jersey. He urged approval of a $67-million-dollar college bond issue.

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Editorial

the challenge we face

The truly professional association functions for the members of the profession—rather than for members of the association only. This is just one of the characteristic differences between the professional association and the trade union.

Members of the profession who are not members of the association typically receive an unearned increment of professional, social, moral and economical gain from the work of their colleagues in the association.

Those who remain outside the organization are the "free-loaders"—they do not pay their way, either in dues or in kind. Unfortunately it is true that the free-loaders in a profession often do not see themselves as such. They do not realize that they are nonpaying and nonparticipating beneficiaries of the sustained work done by those who make up the association representing their profession.

Yet they are in much the same position as citizens who would avoid paying taxes and taking part in public service while benefiting from the taxes and activities of the rest who contribute to the commonwealth.

It is the task confronting every professional association—including pharmacy—to convert *the free-loader* into *the member*, preferably an actively participating member. In that way not only may he do his share of the work which the organized profession needs to have done but his voice also may be heard when the organization formulates its policies.

Sociologists use the term "completeness" to describe this objective.

No professional association has achieved completeness; but among the health professions, dentistry, as we cited in our October editorial, "Salute to the American Dental Association," has a record of accomplishment which represents a challenge to every voluntary association.

Dentistry with 90 per cent and medicine with 60 per cent "completeness" are able and *do* speak effectively for their respective professions. Pharmacy with less than majority "completeness" frequently has difficulty in being recognized.

If pharmacy is to increase its stature as a profession and be given a greater voice in public and interprofessional councils at the national level, THIS ASSOCIATION must achieve a much higher degree of completeness.

The goal which we describe presents as formidable a challenge to the membership of our ASSOCIATION as did the task which faced our nation's founding fathers and their loyal supporters. However, the fruits of accomplishment can be as sweet for pharmacy as they were for the advocates of life, liberty and the pursuit of happiness.

The members of this ASSOCIATION are not unfamiliar with the sacrifices involved in personal acceptance of individual professional responsibility. The generation which preceded us made possible the American Institute of Pharmacy—a professional landmark which has earned pharmacy worldwide recognition. Our present membership has demonstrated the courage to undertake the erection of an office annex which will house the professional and scientific activities required currently and in the future by the profession.

While the physical plant is a basic essential, the key factor to providing the services required by the profession is a competent and adequate association staff. The membership through its organizational process is responsible for chartering association policy and course, but timely implementation of program is a staff function.

In recent years the budgets of the ASSOCIATION have largely reflected increased costs of operation. The ASSOCIATION has utilized annually its full income for the benefit of the profession. By conserving its modest reserve and living within its income, the ASSOCIATION has wisely preserved its credit standing without which we could not have undertaken our present construction program.

Unfortunately, the financial growth of the ASSOCIATION has not kept pace with the program requirements of the profession. Even the most cursory examination of present and future needs clearly indicates that a drastic reduction in free-loaders and a substantial increase in support from our members will be required.

We are confident that in American pharmacy today there are men and women who will accept this responsibility and the opportunity to add substantially to the professional heritage which they received.

our obligation to student branches

In 1928 at the annual meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION, held in Portland, Maine, Dean Charles W. Johnson, in his presidential address called for the organization of student APhA branches at each college of pharmacy in the U.S. and emphasized that "student membership and student branches constitute a problem of major importance to the welfare of THIS ASSOCIATION." Then in 1930, at a joint meeting of the Council of APhA and the AACP executive committee, a plan for the organization of student branches was approved and the program officially launched, even though "unofficial student branches" already were in existence at that time at several colleges of pharmacy. Included among the first student branches were the University of Florida, the University of Wisconsin, the University of Pittsburgh and the South Dakota State College, all activated in 1931 or 1932.

Until 1935 there was little activity in developing student branches, but about this time Dean Ziefle of Oregon and Dean Ernest Little of Rutgers, along with APhA Secretary Kelly began to stimulate the colleges to establish branches. In 1937, Dr. Kelly wrote, ". . . it is apparent that the future of pharmacy rests more than ever in the hands of students and graduates of our colleges of pharmacy. Our sole purpose is to provide a professional organization for them. The student branches represent the best means of bringing into APhA membership of the type of pharmacist that we need."

Since 1942 there has been an ever-increasing number of student branches until today there is a student APhA branch established in everyone of the 76 accredited colleges of pharmacy in the U.S. Reporting on student branches in THIS JOURNAL in 1956, Dean John F. McCloskey noted that "the student branches have stirred the pharmacists in every area where they serve. They have accomplished things that no others could have done. They have given all pharmacists hope for the future and all are proud of them."

We have observed with encouragement the increased interest demonstrated by students in contemporary problems of the profession. We have also observed an undeveloped opportunity for individual members of the ASSOCIATION to enhance the efforts of student branch leaders in developing professional esprit de corps among their classmates.

The presence of active ASSOCIATION members at student branch meetings we believe would have a salutary effect on the entire student body. It would encourage students to recognize that their enrollment in a professional school involves an obligation that extends beyond successful completion of the required curriculum.

A sincere display of interest in student branch programs by active ASSOCIATION members would also demonstrate to deans and faculty members that their efforts in helping students become acquainted with the importance of ASSOCIATION activities and membership is appreciated by the profession.

death takes auxiliary secretary

It is with sincere sadness that we report the sudden death of our recently elected secretary, Anita Birmingham, 39, of Seattle, Washington, at her home Saturday, November 7. A resident of Seattle since childhood, Anita was a graduate of the University of Washington and served as a first lieutenant in the Army Hospital Dietetic Corps from 1945 to 1947. She also worked at Harborview and Doctors Hospitals as well as at the Virginia Mason Clinic. Mrs. Birmingham was a past president of the Seattle Chapter, American Dietetic Association and a member of the American Association of University Women.

Her interest in pharmacy was continued as evidenced by her membership in the Washington State Pharmaceutical Association as well as in the Women's Auxiliary of the AMERICAN PHARMACEUTICAL ASSOCIATION, where she had served as district chairman before her election as secretary last August in Cincinnati. Two years ago she was treasurer of her state auxiliary.

Always active and vivacious our lovely Anita had seemed in very good health and her death comes as a great shock to her family and many friends.

She is survived by her husband, Joseph Birmingham, chief pharmacist of the Veterans Administration Hospital in Seattle, as well as three sons, James, Thomas and Richard, aged six, eight and ten, her mother and two brothers.

According to the wishes of the family, the Women's Auxiliary of the AMERICAN PHARMACEUTICAL ASSOCIATION will make a donation to the Heart Fund in her memory.

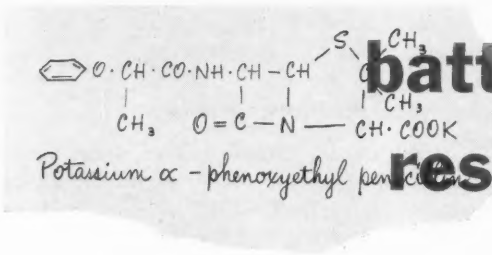
Again, in the name of the officers and members of the Auxiliary, we wish to extend to her family and friends our sympathy and express our own sorrow at her death.

Her funeral took place on November 10, in Seattle at Hoffner's Fisher-Kalfus Funeral Home with burial in the Veterans' section, Washelli.——*Mrs. W.P. Cusick, president, Women's Auxiliary.*

seasons greetings

As 1959 fades away we look forward to a new year, the 108th in the history of our ASSOCIATION. From the entire staff of the AMERICAN PHARMACEUTICAL ASSOCIATION here in our Nation's Capital we extend to all our members the greetings of the season and our very best wishes for good health, happiness, prosperity and the continued opportunity to serve the people of America in the quest for better community health.

New synthetic penicillins for ▪ ▪ ▪



battle against resistant bacteria

SINCE the introduction of antibiotic medication and particularly penicillin, resistant strains of staphylococci have emerged which are virtually impervious not only to penicillin, but to other antibiotics. These staphs can cause epidemics of boils and abscesses, atypical pneumonias and septicemias, which can occur, often fatally, among infants in hospital nurseries. In addition to infections caused by resistant bacteria, allergic reactions to penicillin have been increasing. Although the resistance problem has revolved mainly around *Staphylococcus aureus*, other organisms, such as aerobacter and pseudomonas bacteria, for example, once rarely troublesome, seem to be turning virulent.

The need to find new and better antibiotics has, of course, been recognized for years. By 1958, there were 19 different antibiotics being made and used for medical purposes in the United States. At the same time, another kind of hunt has been in progress.

In spite of its drawbacks, where penicillin works, it still is considered the best drug to put to work. Against rheumatic fever, gonorrhea, syphilis and pneumonia, for example, and even in staph boils unless resistant strains are present, it is considered the drug of choice. Where it works, it works dramatically; no other antibiotic works so fast and efficiently. Except for the sensitization problem, it is a phenomenally atoxic drug.

One of the best hopes for continued success in the war against microbes has seemed to lie in finding a way to rejuvenate penicillin, of finding means to synthesize the compound, change part of its structure, develop new compounds which might have the natural drug's basic good qualities coupled with needed new characteristics.

Today the seemingly impossible has become actuality as the result of two happy feats, one in Britain and one in the U.S., and a working combination of both that has moved rapidly, producing striking results in less than half a dozen months.

Since 1928, when Alexander Fleming noticed in his laboratory that a penicillium mold had contaminated a culture dish and inhibited germs around it, 15 years were to elapse before penicillin came into wide medical use. Fleming's work—his subsequent preparation of a crude concentrate, his finding that it stopped growth of certain germs and his publication of the finding—was ignored until World War II presented desperate emergencies in military infections. Then, in an Oxford laboratory, Sir Howard Florey, his wife, and Dr. Ernst B. Chain, a German refugee, worked feverishly to extract an active substance from *Penicillium notatum* molds. The tiny amounts they could produce were enough for a time to sustain a London bobby dying of an overwhelming infection, but there was no more to save him when he had a relapse.

In 1941, Florey came to the U.S. to ask for help in producing penicillin. The committee on medical research of the Office of Scientific Research and Development organized government agencies, universities and pharmaceutical companies to attack the problem. Penicillin was in mass production in 1943, in time to play an important role in winning the war. Deep tank fermentation was the method of production, the only method. Synthesis was tried then and continuously since then.

John C. Sheehan, with several years of unsuccessful effort to solve the penicillin synthesis problem behind him, in 1948 started a new approach. The penicillin molecule contains a four-ring system found in no other natural product; it is a beta lactam ring system with each ring having three carbon atoms and one nitrogen atom. Sheehan would try to synthesize the four-ring nucleus with only simple side chains attached.

Finally, in 1950, Sheehan had managed to synthesize a 5-phenyl-penicillin. It turned out to be inactive. Sheehan went back then to check the technics he had been using to hang substituents onto beta lactam. He had to find new ways of closing the ring,

Pilot plant fermentation operations at Bristol Laboratories in Syracuse, N.Y.

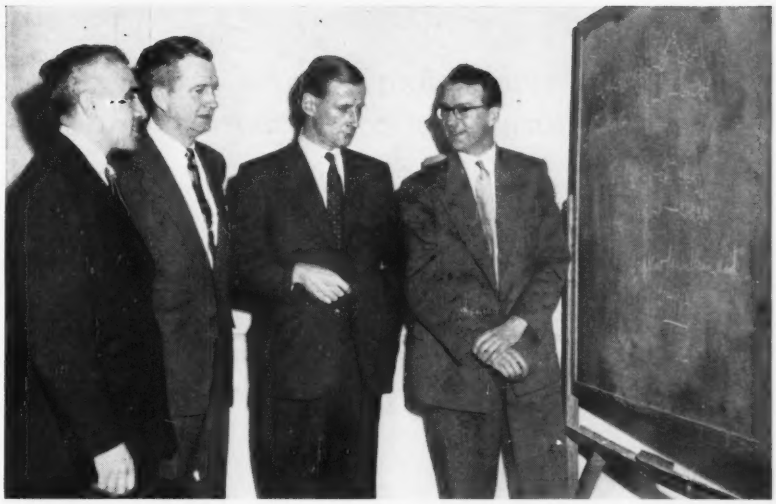
he decided. He found the right ones finally in 1957 when he succeeded in producing penicillin V, synthetic all the way. But, while synthetic penicillin V was a creative feat, a chemical victory, it was not a practical one. The steps to synthesis were too many and too costly.

In arriving at penicillin V, Sheehan had discovered methods which would allow the synthesis of new penicillins. The technics were complicated and costly but did allow the synthesis of a dozen or so variations. One of the dozen turned out to be effective against a staphylococcus resistant to natural penicillin. None was sufficiently striking to warrant commercial production but there were many more to be tried. Sheehan recognized that if one could obtain another interesting intermediate, namely 6-aminopenicillanic acid (6-APA), it would allow the ready synthesis of an unlimited number of new penicillins. He went on next to convert a natural penicillin, penicillin G, into 6-APA. Now, it became possible to partially synthesize new penicillin compounds by removing the side chain from a natural penicillin and replacing it with a different chain. The recognition of the possibilities of synthesis of new penicillins through 6-APA was at this time an intriguing but a frustrating realization because of the difficulty of obtaining sufficient 6-APA through synthetic methods.

British investigators of Beecham Group, Ltd., were able to announce early in 1959 that a fair amount of 6-aminopenicillanic acid, the nucleus of penicillin, was present in the fermentation broth along with the whole penicillin. Apparently the mold made 6-aminopenicillanic acid in the process of making penicillin; and in *Nature*, **183,** 257 (Jan. 24, 1959), a British group, F.R. Batchelor, *et al.*, reported that they had succeeded in stopping the natural fermentation process immediately after formation of the nucleus and were taking out 6-APA quite simply by ion exchange.

In March, the editor of *Lancet*, **1,** 508(Mar. 7, 1959) observed that the consequences of this discovery "could be far-reaching. Already there are indications that it will be possible to produce readily penicillins which do not cause reactions in penicillin-sensitive patients . . . New approaches to the problems of the resistant staphylococcus should now be feasible, and means may be found for enhancing the activity of penicillin-type compounds against the Gram-negative bacteria."

A team of British scientists (F.P. Doyle and G.N. Rolinson) and Americans (J.C. Sheehan and Amel R. Menotti) at Bristol Laboratories have utilized a combination of the British fermentation method for producing 6-APA and the American technic of attaching side chains to it to prepare more than 500 new compounds. Already, more than 60 out of hundreds of the new penicillin compounds synthesized have shown sufficient virtue to lead to preliminary clinical trials.



Bristol research team (l. to r.) A.R. Menotti, J.C. Sheehan, G.N. Rolinson, and F.P. Soyle discussing modified penicillins.

About to be released for widespread clinical use [FDA released Nov. 6, 1959] is the first of the "unnatural" penicillins—potassium penicillin-152 (Syncillin, Bristol), made by interacting DL-alpha-phenoxypropionic acid with 6-APA. It is a mixture of two therapeutically complementary stereoisomers of the chemical alpha-phenoxyethyl penicillin. Chemically, Syncillin has a structure similar to that of penicillin V, but contains an additional methyl group. It is this added CH_3 which provides the asymmetrical carbon responsible for the stereoisomerism.

Syncillin is a colorless, crystalline material which is very soluble in water but relatively impervious to decomposition by acids. The drug is not hygroscopic, and is not appreciably affected by air or light. Given orally, it appears to be more potent than penicillins V or G, and provides twice the blood activity of potassium penicillin V and higher blood levels than those normally obtained with penicillin G given by intramuscular injection.

It resists destruction by the enzyme penicillinase to a greater degree than other penicillins which may explain why, in *in-vitro* tests, the drug destroys many clinical isolates of staphylococcal strains resistant to other penicillins.

Detailed information on the composition, standards of potency and purity, and the certification of potassium penicillin-152 (Syncillin) and its dosage forms (tablets, and powder for oral solution) was published by FDA in *Federal Regulations* **24,** 9263 (Nov. 14, 1959).

The efforts of the British collaborators in this exciting victory in man's war against disease are rewarded by the release of Broxil (BRL 152), the potassium salt of 6-(α-phenoxypropionamido)-penicillanic acid from Beecham Research Laboratories, Ltd., to the medical profession for further clinical evaluation of "the first of the new penicillins." The U.S. translation of the British chemical name is potassium α-phenoxyethyl penicillin.

On October 13, 1959, Pfizer announced that its biochemists, H.T. Huang and T.A. Seto, independently had obtained a synthetically-modified penicillin called Maxipen. *Chemical & Engineering News*, **37,** 25(Nov. 2, 1959) states: "Maxipen is made by first producing 6-aminopenicillanic acid 'by a unique Pfizer process,' then synthetically linking α-phenoxypropionic acid to this molecule." A Pfizer spokesman confirms that Maxipen, one of its more than 1200 compounds synthesized, is structurally identical with Bristol's Syncillin.

With the penicillin nucleus now available for easy synthetic modification, the possible results include less allergenic penicillins, broader spectrum derivatives, and penicillins effective against mutant forms or surviving forms of bacteria resistant to other penicillins. Here again is a challenge to the pharmaceutical industry to spend millions of dollars in the synthesis, processing, and testing of many new compounds in their constant efforts to produce better therapeutic agents.

It is evident that here is a significant development in the field of antibiotic production, and it could be an important contribution to the advancement of the general knowledge of chemotherapy. ■

a symposium on the processes of pharmaceutical manufacturing

practical pharmacy in

introductory remarks

*by William H. Schaeffer**

William H. Schaeffer, merchandising manager of the Wm. S. Merrell Company, has spent 24 of his 40 years in pharmacy. A graduate of the University of Cincinnati, college of pharmacy, he worked in retail pharmacy prior to World War II. Returning from service in 1945, he joined Merrell as a medical sales representative. In 1952 he became assistant sales manager and moved up to merchandising manager in 1956. On October 1 of this year he took over the post of division manager of the St. Louis sales division. He is an active member of the Cincinnati Sales Executive council and the APhA Cincinnati branch.

THIS symposium presents a few of the more important processes concerned with practical pharmacy in industry and discusses briefly six various departments of pharmaceutical manufacturing.

In this day of increasing costs and increasing government interest in costs, it behooves us as pharmacists to place our story of the value of pharmacy before the consuming public. Few industries support as much research, complex production and quality control

* Merchandising Manager, The Wm. S. Merrell Company, Cincinnati 15, Ohio, who served as moderator of the Symposium presented at the APhA Cincinnati 1959 meeting.

raw materials flow

by Ralph Montgomery

THE NATURAL sources of some of our raw materials are in India, Africa and the Near East. Karaya crystals, which we use in the manufacture of Bassoran, come from India. Acacia, used in lozenges and other products, comes from the Sudan. Tragacanth ribbon, used in lubricating jelly, comes from Iran.

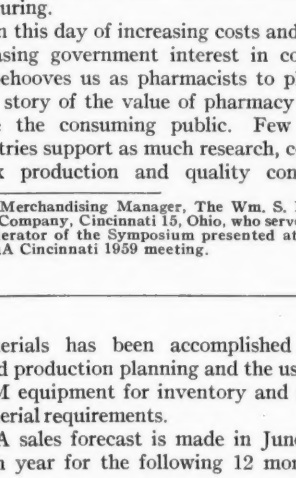
Some European countries and Japan can produce certain raw materials at a lower cost than they can be produced in this country. However, most buyers are supporting manufacturers in this country and purchase from 50 per cent to 90 per cent of their requirements here.

We use a total of approximately 450 different chemicals in the manufacture of our products. Materials arrive at the plant from the first to the 15th of each month for use the following month. We have a turnover of raw materials $4^1/_2$ times per year as compared to the normal or usual of three times per year.

Our inventory costs have been reduced due to this more frequent turnover. If, for example, our total yearly cost of raw materials were one million dollars then a turnover of $4^1/_2$ times per year instead of three times would result in a savings of approximately $22,000 per year.

This more frequent turnover of raw materials has been accomplished by good production planning and the use of IBM equipment for inventory and raw material requirements.

A sales forecast is made in June of each year for the following 12 months



Ralph M. Montgomery is a graduate of the University of Minnesota, where he majored in mechanical and industrial engineering. Before joining the Wm. S. Merrell Company in 1945, he had received wide experience in various fields of industrial engineering. Currently in charge of methods engineering at Merrell, he is active in the MTM (Methods-Time-Measurement) Society.

in industry . . .

costs as pharmacy—yet pharmaceuticals are modestly priced—and with no help from tax favors or government subsidies. Still, it is difficult for some consumers to understand why 12 life-saving tablets should cost as much as a fifth of bonded bourbon. Even you and I fail to consider that, on an average, we spent more for the new car we purchased this year than we will on prescription medications the rest of our lives.

Most competitive pharmaceuticals in the manufacturers' catalog in 1947 still carry the same or even lower wholesale prices today. Many price reductions have been extremely dramatic. I recall a product package that sold for $10.80 wholesale in 1947—today the same package *of even greater quality* can be purchased for 22 cents. The pharmaceutical industry is unique in that its products normally go down in price and increase in quality as they remain in the market.

The pharmaceutical profession has made vast strides in the past 20 years—strides that have given us products of peak quality at minimum cost—strides that have given this nation the finest public health picture in the history of world civilization. This could not have occurred if profit motive *alone* had been the consideration. Men of pharmacy, solving the day to day problems of practical pharmacy in industry, contributed much to our advances.

Each author emphasizes the importance of cost and quality control. Such emphasis on product quality and low consumer cost is a credit to pharmacy in industry—an industry that spends millions a year in research to make its present products obsolete and man's life span longer. ■

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and this is reviewed every three months for possible revisions. Batches of products are planned ahead for each month, based on this forecast. IBM cards are punched for each product indicating the amount of each raw material required for a batch. An IBM report is made, based on the planned batches, showing the raw material requirements by month for the next six months.

Perpetual inventory records are also kept with the IBM machines for each raw material. By keeping a close control on our inventory and accurately determining our future needs we are able to have a more rapid turnover of raw materials.

receiving and storage

When material is received at the plant the weight of each container is checked and a receiving ticket and disbursement tags are made out for each manufacturer's lot number received. One tag is made out for each container and a master disbursement card is made out for each lot of material. Records of disbursements are kept on the master card only. The purchase order number of each lot of material is used as the lot number and this number is always shown when the material is used.

Raw materials are held in the receiving area until the control laboratory has taken samples and okayed them for use. *U.S.P., N.F.* and certain other tests are made to assure that the raw materials meet Merrell specifications. The control department determines the strength of each lot of material and marks it on the disbursement card if it is over or under 100 per cent. The disbursement tags must be stamped with the control laboratory "OK" before the material can be used for manufacturing purposes.

After the material has been okayed, it is moved to the drug storage area.

Our raw materials are received in a large variety of package sizes and shapes. Some materials are stored on pallets and handled by an electric fork truck. Small quantities in small package sizes are stored on shelves. Poisons and other dangerous chemicals are stored in locked areas.

Sorbo, glycerin and glucose are received in tank cars and trucks. We have made considerable savings in

Raw materials arrive from everywhere.

Raw materials properly stored until required.

handling time by purchasing these materials in tank cars and trucks instead of 50 gallon drums as previously done.

The material is pumped from the tank car into storage tanks and from storage tanks into the mixing tanks as needed. The storage tanks are calibrated and the material is metered into the mixing tanks.

dispensing

When a batch of a certain product is to be made, the formula is sent to the drug room. The material is accurately weighed according to the formula and the amount and lot number of each material is shown on the formula. If a material is over or under 100 per cent strength, as determined by the control laboratory, the equivalent weight at 100 per cent is calculated and weighed out. These calculations are checked in the control laboratory. The formula is then sent to the control laboratory where the weights and lot numbers are checked. The weighed materials and the formula are sent to the manufacturing department.

The department supervisor reweighs the materials to make sure that errors have not been made. At this point the raw materials are ready to use in the manufacture of a batch of a product. ■

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liquids manufacturing

by T.H. Brown

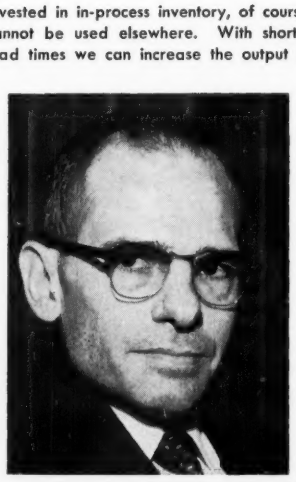
PROCESSES involved in liquids manufacturing are as simple as mixing alcohol and water, as complicated as time and temperature controlled chemical reactions. Other processes commonly used are homogenization, emulsification, filtration and particle reduction. For mixing, we use tanks ranging in size from 50 gallons to 2,000 gallons, either stainless steel or glass lined; most of them are jacketed for heating or cooling. *Homogenization* is done by mills using the principle of rotor and stator with close tolerance ground surfaces. *Particle reduction* is a similar process frequently used in processing to provide a creamy, uniform suspension of insoluble material. *Emulsification* can be performed with any of several types of high speed agitators plus the use of a homogenizer or colloid mill. *Filtration* processes range in volume from that obtained by a funnel and paper to several thousand gallons per day delivered by plate and frame filter presses.

The volumes and weights of materials handled range from a few centimeters of a flavoring oil to 2,000 gallons of bulk liquid, from a few grams of a dye to granulated sugar by the ton. To mix these smallest and largest quantities, we use agitator motors ranging in size from $^1/_{32}$ hp to 15 hp, with blades from a half inch to three feet in diameter.

A really effective cost control program is one which produces the desired effect on costs but, at the same time, maintains or improves quality. A lowering of quality to reduce costs will not increase profits over the long range. Our efforts in the area of cost control have been directed as follows:

1—Wherever sales and inventory policy will permit, we have increased batch sizes. In the last ten years we have progressed from maximum batch sizes of 500 gallons to 2000 gallons.

2—We have reduced manufacturing lead time by process and equipment improvements and more careful scheduling. Money invested in in-process inventory, of course, cannot be used elsewhere. With shorter lead times we can increase the output of



Tom H. Brown, production superintendent at the Wm. S. Merrell Company, received his BS degree in pharmacy in 1937 from Kansas University and has done postgraduate work in bacteriology. For 20 years he has been engaged in pharmaceutical manufacturing.

existing equipment and postpone the time when additional capital must be expended for tanks and other equipment.

3—The use of more efficient equipment has reduced the manpower requirements, the in-process time and floor space required. In recent years we have installed larger and more efficient filter presses, larger mixing tanks with more efficient heating jackets and larger homogenizers and have automated wherever possible.

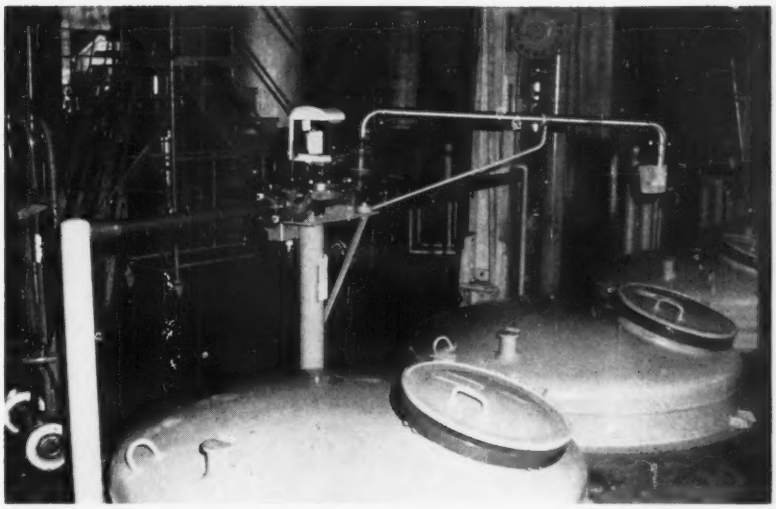
4—Great strides forward have been made in materials handling methods. When making several thousand gallons of liquid each day, not only are large volumes of water involved but, depending on the product mix, tons of sugar, hundreds of gallons each of glycerin, liquid sugar, alcohol and glucose must be handled. To reduce materials handling time and the manpower required, electric hoists on tram rails are used for handling drums, heavy pieces of portable equipment, etc. Whenever practical, raw materials, such as alcohol, glycerin, glucose and sorbo, are purchased in tank car quantities, stored in 6,000–12,000-gallon storage tanks and pumped to the manufacturing department where the proper quantities are automatically metered into the mixing tanks.

5—Many old products eventually shrink in volume to the extent that they no longer can be fitted to present equipment. When the volume falls and it is no longer profitable to keep such products in the line, their deletion indirectly provides equipment and floor space which can be used more efficiently for larger volume new products.

6—Even with the best manufacturing technics, a shrinkage of inventory results from residual material in pumps, hose lines, pipes, filter presses, etc. In recent years, we have carried out a program to reduce these manufacturing losses and have been successful to the extent of several thousand dollars per year in the improvement of bulk product yield.

7—The opportunity for using automation in the manufacture of liquid pharmaceuticals is somewhat limited. We have, however, applied it successfully to one product. We combine four automatically proportioned liquids to produce the final product. The manufacturing rate is controlled by the rate of packaging to provide a constant supply of bulk liquid to the bottling lines.

8—Production planning and scheduling have been improved to provide a more accurate forecast of production requirements extending further into the future. Such planning enables us to make more efficient use of manpower and equipment and to plan longer product runs for real economy. Set up and clean up time is the same for a 10,000- or a 5,000-gallon run. Longer range planning helps us to schedule around equipment bottlenecks and frequently avoids the necessity for purchasing duplicate equipment.



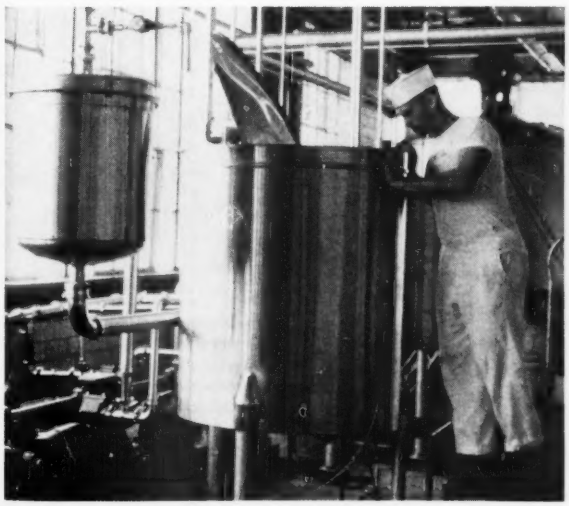
Mixing vats for liquids.

Such steps as these have enabled us in the last seven years to increase the production per man hour by 173 per cent. One liquid, presently made in large volume, required eight-man hours to produce 500 gallons 15 years ago. It now requires a half-man hour to produce 14,400 gallons.

Quality control—one of our most important activities—is exercised principally by two departments, the manufacturing department and the analytical and control. Manufacturing personnel assist in maintaining quality by such means as good sanitation practices, accurate color matching, good filtration technic, and accurate compounding methods. These people must be well trained and have proper supervision. Both the supervisor and his people participate in training programs to broaden their knowledge of new methods and ideas, and to improve their job performance. They are kept well informed as to company policies and objectives, all of which contribute, indirectly at least, to good morale and better workmanship.

Control checks include the identity and quantity of each raw material, the addition of each raw material to the batch, inprocess checks by the analytical and control department, check-off of each manufacturing step, a final volume check, germicidal tests, bacteria counts, chemical assays and physical checks—such as color, viscosity, specific gravity, centrifuge tests, etc.

While liquids manufacturing may not be as dramatic as certain other activities in the drug industry, it has some very interesting aspects. Changes in this area are being brought about through the rapid growth of the industry, new developments in equipment and methods and new liquid vehicles and dosage forms. ●



Complete unit for a liquid product.

Powder mixing for granulation.

tablet manufacture

by Eugene Walters

THERE are several methods of preparing materials for compressing into tablets in general use today. All materials, both active ingredients and diluents, must first pass control tests. They are then weighed out for each batch in the drug room and delivered to the production department. Here the weights are again checked and the materials placed in z-bar mixers of the proper size. After thorough mixing to insure distribution of the active ingredients with the diluents, a granulating solution is added until a uniform mass is produced. The granulating solutions used vary according to the product being produced. This solution serves two purposes—*first*, it adds a binding quality to the powders so that the final tablet will stick together; *second*, it changes these powders into a granulation which will be free flowing when placed on the compressing machines.

It is of utmost importance that the batch size be as large as possible and the final tablet as small as possible because this cuts down on the number of control assays required and gives a maximum number of tablets for the same amount of labor. This way we are able to keep the final cost per tablet to the patient as low as possible.

After granulation, the wet mass is passed through screens of various sizes onto trays and placed in ovens to dry. After drying, the material is put through screens of proper size. This size depends on the size of the final tablet—the smaller the tablet, the smaller the screen used for dry grinding.

The dried granulation is then placed in a mixer, such as the Paterson-Kelley V-type, mixed and a lubricant added. A lubricant is needed to make sure the tablets do not stick to the punches and will slide out of the dies all in one piece with a good, smooth finish. Sometimes the lubricant can be added at the time of granulation. This is done whenever possible on materials that do not require much lubrication, because it eliminates one step in the manufacturing process and reduces the final cost of the tablet. This is called internal lubrication. At the time of lubrication when the tablet must disintegrate rapidly, a disintegrating agent may be added. The most common of the materials used is starch.

This final granulation is then placed on tablet compressing machines where the tablet is formed. There are all different sizes of compressing machines from a single punch which will produce 75 to 150 tablets a minute to 41 station machines which will produce from 2000 to 3000 per minute. In order to keep production costs at a minimum, we try to formulate granulations which lend themselves to high speed compressing. This means that the tablets are under compression only a fraction of a second and still must hold together and result in an elegant-looking and otherwise satisfactory tablet.

Some tablets require coating for various reasons—*To protect from moisture, air and light; to mask taste, odor or appearance when necessary; to protect the active ingredients from reaction with the gastric juice in the stomach.*

These must be coated in such a way as to prohibit them from disintegrating in the stomach but allow them to disintegrate in the intestine. These are called enteric coated tablets. Active ingredients may be placed in the sugar coat which would dissolve in the stomach for quick action and the compressed tablet inside the enteric coat would be released later in the intestine.

The application of the conventional sugar coat is time consuming. The tablets are placed in large coating pans which rotate from 30 to 36 times a minute and various coating solutions are added in shots in the desired size and color. They are then polished with wax to protect them from moisture. This process normally takes from four to five days from each pan load. We have been able to reduce this to two or three days by changing the shape of the compressed tablet and using different coating solutions.

Film coats have recently been developed which reduce the size of the final tablet and can be applied in a much shorter time. Press coating is a new and much faster method of coating tablets where there is a need to protect the active ingredient from the elements. This is done by preparing core tablets containing the active ingredient and passing these tablets through a compressing machine a second time, placing the core exactly in the center of a tablet. The outside tablet may be made of a sugar base granulation but

E.L. Walters, a member of APhA and a graduate of the University of Cincinnati, college of pharmacy, has an extensive background in the development of new pharmaceutical dosage forms and combinations. For the last 15 years, he has been associated with the Wm. S. Merrell Company where he is senior pharmaceutical chemist.

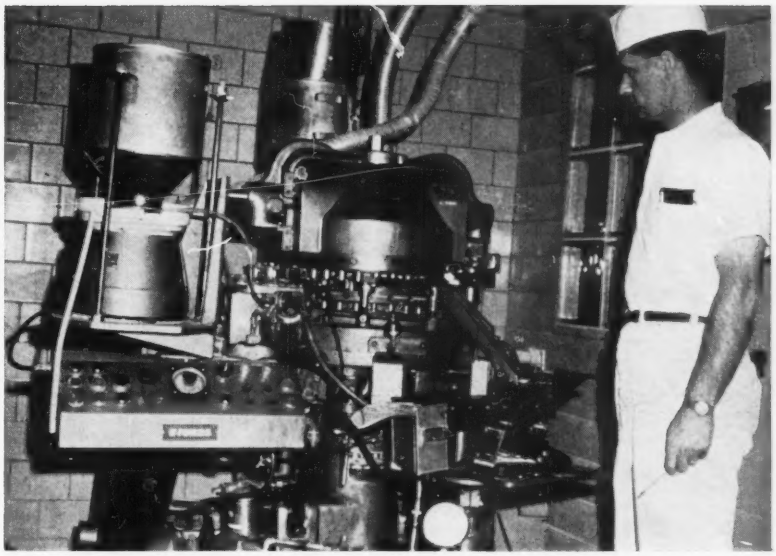
can have active materials in it as well. Special machines are required for this operation.

There are some materials which will compress into tablets without granulating. Examples of these materials are sodium chloride and ammonium chloride.

Other materials which are sensitive to water are sometimes mixed and compressed into large tablets These are then ground to the proper size and recompressed. This process is called slugging.

We have recently developed a new process for granulating which we believe will reduce the time, labor and cost of tablet manufacture. This process was reported at the Cincinnati Convention of APhA. In this process the materials for granulating are placed in a large coating pan equipped with baffles and a variable speed drive. The pan is first rotated to mix the ingredients. The granulating solution of choice is then sprayed on the powders, under pressure, while the pan is in motion. After the granules are formed heated air is passed into the pan over the granulation while the pan is rotating at a slow speed. When dry, the lubricant is added and the granulation passed through a screen of proper size. This granulation is then ready for compressing. As can be seen this process eliminates a large amount of labor and storage space and is much faster than the conventional methods.

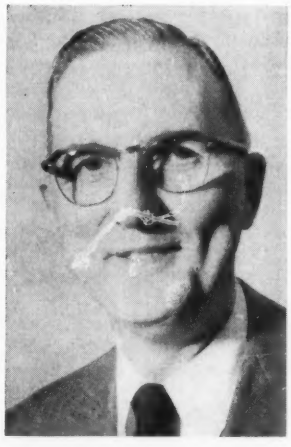
There are other types of tablets used in pharmacy. An example is molded tablets, most of which are used for hypodermic injection. These tablets are composed of all soluble materials. The materials are mixed and reduced to a fine powder then wet down with alcohol-water mixtures and pressed into plates while wet. After ejection from the plates or molds they are dried. This process can be done by hand or by machine.



High speed tablet production.

There are many control checks and assays necessary during the production of tablets for pharmaceutical use. Each of the raw materials must be assayed before they can be used. Physical tests must be run on each batch of tablets and each active ingredient must be re-assayed in each batch of final tablets to assure each and every tablet's having the proper dosage.

As can be seen, the pharmaceutical industry is constantly trying to improve production methods always with the objective in view of increasing production rates and reducing the cost of the final product to the patient. ■



Arthur J. Rosemary has been in charge of the parenteral and narcotic department of the Wm. S. Merrell Company for 13 years. He is a graduate pharmacist of the Philadelphia College of Pharmacy and Science and was with Merck Sharp and Dohme and the Federal Drug Administration before joining Merrell. He is a member of APhA, the American Chemical Society and Parenteral Drug Association.

parenteral manufacturing

by Arthur Rosemary

THE PRODUCTION of parenteral medication plays a vital part in American medicine today. With the present trends in formulation and product development there is every indication that the use of parenteral solutions will be increased and we can expect more and more emphasis to be placed on this class of pharmaceuticals.

There are eight major categories in the preparation of parenterals—compounding of solutions and their filtration, the washing of containers, the filling and sealing of containers, their sterilization, testing and inspection and finally packaging. Of course, of absolute necessity is the function of control, both physical and chemical.

Various methods and equipment developed in recent years have greatly reduced the manual labor required in the compounding of injectable solutions. We have progressed from the stoneware crock to the glass lined kettle.

Virtual elimination of the hazard of pyrogenicity has been one of the outstanding achievements in the field of parenteral therapy. This has been brought about by a more complete knowledge of the nature of pyrogenicity together with a rigid aseptic technic now used in the preparation of these products, from the water used to the final product.

Water stills have been improved to prevent the possible entrainment of pyrogens which may be in the feed water. The water from the still is continuously checked on a recording micromax which gives a constant check on the satisfactory operation of the still. Sterilizing of the water storage tank

is performed each morning before any water is collected for manufacturing. Samples of the water are taken each day and submitted to pharmacology for pyrogen test before being used in manufacturing. This water is sterilized and used the following day after completion of the pyrogen test.

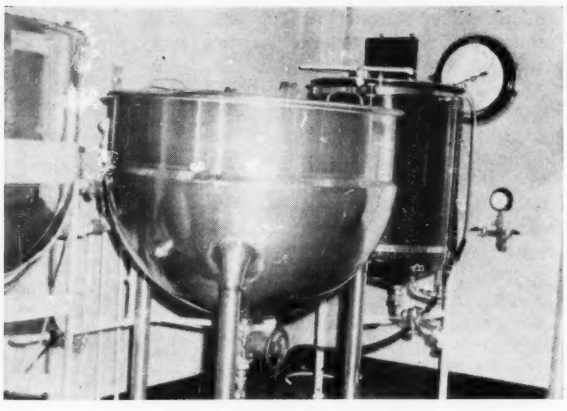
Rapid strides have also been made in the field of clarification or filtration. We have found that the clarity of parenterals is largely dependent on the environment in which they are produced. We think in terms of scrupulously clean areas, filtered and ultraviolet treated air, dust-free equipment and, above all, personnel who are conscious of their clean, white uniforms and the importance of their jobs.

As clean, sterile air is essential in obtaining the optimum condition for satisfactory production, every precaution is taken to maintain air as clean and as near sterile as possible, with comfortable working conditions for the operators, using the latest equipment available for this purpose.

The air filter also has a high efficiency in the elimination of bacteria and mold spores. The air goes to the duct distribution system and passes over ultra-violet germicidal lamps which reduce the bacterial content to a very low count; but a strictly sterile condition can never be attained. Shielded, sterile lamps are also installed in each filling cabinet directly above the filling operation, at the room ceilings.

In addition, the filling rooms are periodically washed down with five per cent phenol solution. So one may say for practical purposes the air is sterile.

Along with the marked advance in design of equipment has evolved the automatic filling and sealing machine.



Sterile liquids for parenterals.

Not too many years ago individual ampuls were washed in baskets, individually rinsed, sterilized, filled and sealed.

Today, ampuls are automatically washed, filled and sealed on machines. Yesterday's production—2,500 units filled and sealed per operator per eight-hour day; today—18,000 units filled and sealed per eight-hour day. Needless to say, this increase has not come about by mere machine, for were it not for the glass industry and their vast improvement in the ware which they have developed and their close cooperation with the machine manufacturer, these high production figures would not have been possible.

Of equal importance is the rubber closure used in conjunction with the multiple-dose vial. There have been developed new formulas in rubber composition, new forms and shapes so as to eliminate the dirt retentive crevices. However, I believe we are still seeking the ideal closure—one that is chemically inert, one that can be easily washed, one which when pierced with a needle will not core and one which will not bleed. During the past ten years we have devoted much time to the study of rubber closures and the various technic used in their washing and I am of the opinion that there are about as many washing technics in use today as there are rubber formulations.

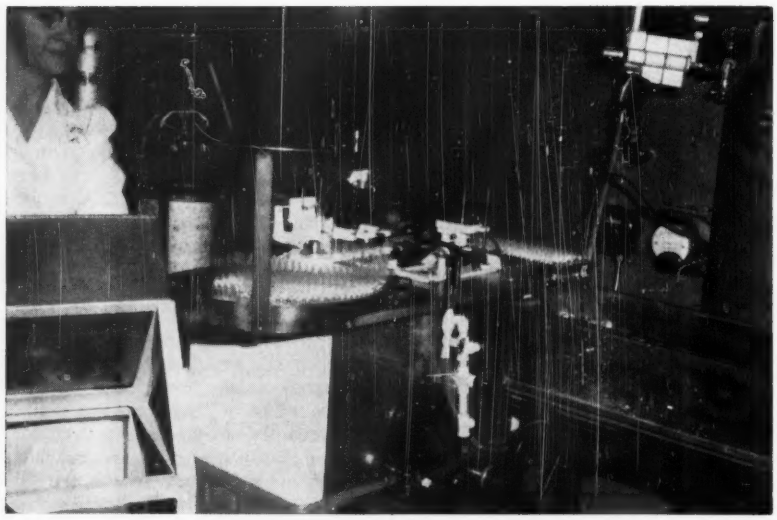
The washed ampuls and vials are sterilized in an electric oven at 380 degrees F for four hours. At this temperature and time they are not only sterilized but the possibility of pyrogen contamination is eliminated as the pyrogenes are destroyed when exposed to this high temperature for this length of time.

Heat labile solutions are sterilized by filtration using the proper filter element. This may be a cylindrical microporous porcelain filter element or bacterial filter pads. All units used in sterile filtration, such as the filter, connections, bottles and air filter are sterilized in the autoclave at 250 degrees F for one hour. This operation is done by a trained technician using a sterile technic. Solutions that are heat stable are filtered for clarification and sterilized in the filled containers at various temperatures and periods of time which vary with the product. The temperature and time used for sterilizing each product is determined at the time the product is developed. All heat sterilized products are compounded filtered, filled and sterilized within 24 hours. Bulk solutions are stored overnight in a refrigerator at two to ten degrees C.

All filled ampuls are placed in a dye bath after sterilizing to detect leakers.

After completion of all tests—the assay, pH, sterility, mold and pyrogen test—the ampuls and vials are inspected against a black background and against a white background with a light which, at a point ten inches below the source, provides an intensity of illumination not less than 100- and not more than 350-foot candle powder. If any undissolved

Ampuling and sealing operation.



material is detected, the ampul or vial is rejected.

Control, both physical and chemical, plays a most important function in parenteral production. Incoming materials require additional assays and tests for parenteral use to insure the safety and stability of the final product. The bacteriology department performs sterility and mold tests on each batch produced, also sterility tests on bulk which has been sterile-filtered before it is released for sterile filling, after which the regular sterility and mold tests are made. This results in 30 sterility tests per batch. They also make plate counts on the filling rooms and microbiological assays on such products as cannot be assayed chemically.

A representative of the control department is assigned to the ampul department with the responsibility of checking the amount of fill before the filling operation begins and periodically during filling. All inspected ampuls and vials are spot checked during inspection and a final check is made when lot is finished. This also includes checking of all records. ■

Special lot filling operation.

modern pharmaceutical packaging

by J.D. Breslin

Not so very long ago, no one had ever heard of a packaging engineer for a pharmaceutical company. Most companies packaged their products with methods that were very similar to those employed in a small pharmacy. The methods used were inefficient by today's standards and the packages were far from elegant.

Today's pharmaceutical package is the result of efforts by many different groups to satisfy many different requirements. Today's package is *engineered* to provide the best possible packaging at the lowest possible cost. As a result of the efforts of these many groups, today's successful pharmaceutical package must be many things.

John D. Breslin, packaging department manager for the Wm. S. Merrell Company, is a graduate of the University of Cincinnati where he received his degree in chemical engineering. Prior to his present position, he was in charge of package engineering. He is a member of the American Institute of Chemical Engineers and a director of the Ohio Valley Packaging Association.

First of all, it must be attractive. If it is a prescription product, it must have a look of quality about it. It must convey the image that it is safe, clean and ethical and that care was take in its manufacture.

If it is to be a successful part of the rapidly growing over-the-counter business, it must retain this quality appearance, but, in addition, it must satisfy the demands of effective modern merchandising. It must look like a better quality product than its competitors, yet give the impression that the customer is getting his money's worth. Its packaging must be appropriate to its contents and use. In short, it must shout "BUY ME" at the passing customers.

Today's successful pharmaceutical package must also be convenient. Packages used for prescription products must be labeled in such a way that the pharmacist can readily identify them.

The packages themselves are selected with their end use in mind. Such features as wide-mouth containers for thick liquids, pour-out finishes for thin liquids, and proper sizing of openings for dispensing tablets are all factors which must be considered.

A package which will be used in the bathroom, or any other area where the user's hands are apt to be wet, should be made of unbreakable material if possible. If it is necessary to make such a package of glass, it should include a grip feature.

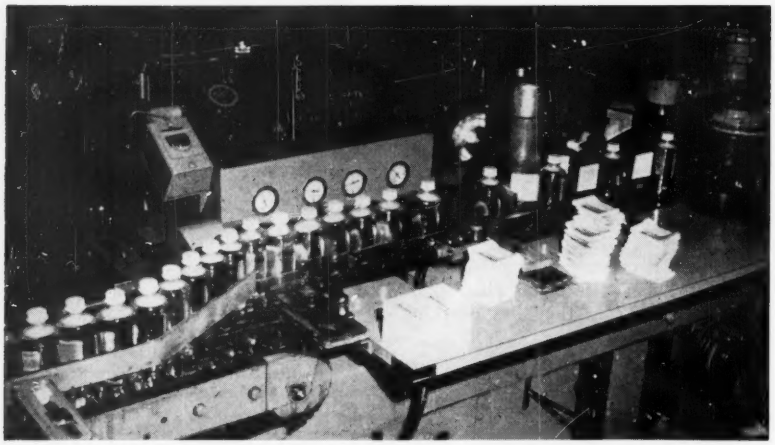
Many of today's pharmaceutical packages have some additional features which enhance their use. One firm markets a liquid aspirin for children, which has a "safety valve;" we have a poison ivy lotion in a roll-on bottle.

Probably the most important requirement of today's pharmaceutical package is that it be economical (but not cheap!). The highly competitive nature of today's business will not support inefficient packaging.

If it were not for the tremendous advances made in packaging technology in recent years, today's drugs would be much more costly.

In a period that has seen the cost of labor and material double and sometimes triple, we have items that sell at or near the same price that they did 10 and 15 years ago. It has been possible to maintain this price position only by tremendous advances in manufacturing and especially in packaging efficiencies.

Advances in machinery have required equal advances in packaging materials. When bottles were filled, labeled and capped by hand, small variations in bottle diameter, height and roundness made little or no difference. Now, however, package materials must be manufactured to a high degree of uniformity if they are to be used on high-speed equipment. If these materials are not uniform, the



Automatic packaging equipment.

equipment simply will not function.

Economy in packaging extends beyond cost of material and packaging efficiency. The package must also be economical to handle, store and ship.

The package in many instances must protect its contents from light, moisture and other contamination or deterioration. This means that special glass must often be used, special moisture absorbing agents may have to be included and all components of the package must be tested to be sure that they do not contaminate the product. These components must also be tested to insure that they are not damaged by the product.

Many packages must provide some type of seal to insure that there has been no tampering or pilferage. These seals range from aluminum to paper, but all must be tested to insure their effectiveness and safety for the packages.

The last requirement of a pharmaceutical package is that it be legal. The labeling of all drugs is subject to regulations of the Food and Drug Administration in regard to copy, layout and prominence of certain statements. Rubbing alcohol may be packaged in one size only and labeling requirements must be strictly followed. Narcotics must have certain markings on the label in a specified color, place, style and relative size and they must be sealed with a narcotic tax stamp.

Both the Interstate Commerce Commission and the Post Office have rules and regulations regarding what may be shipped, how it may be shipped, how it must be packed, how it must be labeled, how big a package may be, etc. In addition, many state and local governments have passed laws regulating the labeling, quantity which may be sold and what may be sold.

Today's successful pharmaceutical package must meet all of these requirements, please all of these diverse groups with their varied interests and still maintain its basic function of conveying useful medicine from the manufacturer to the pharmacist and consumer.

the control function

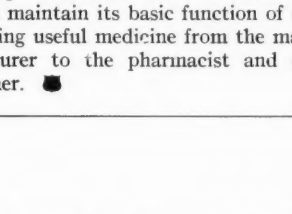
by George O. Sharp

In the pharmaceutical industry the cost of the control function is the price of insurance for good products, some protection against the liabilities of doing business in pharmaceuticals and the building of the reputation of a given company.

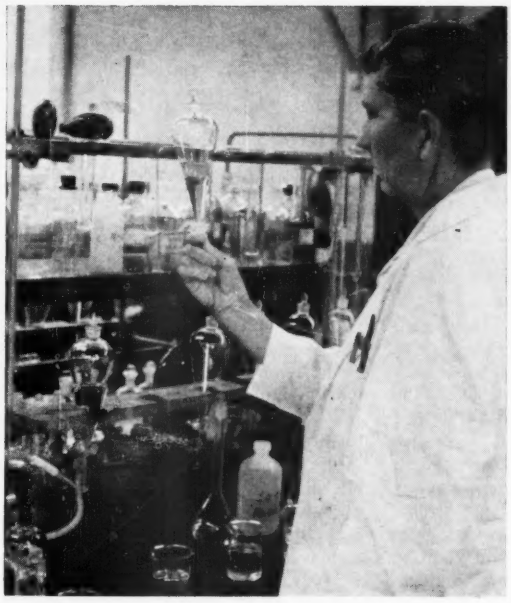
But what do we in a control department do? We first have to decide what we want—whether it be the raw material of a brand new drug or dosage form or a well-established official drug. Is it a fine powder or a coarse granular material? Should it be white or can we tolerate some slight color? Tentative specifications for purchasing are then drawn for the raw material to be purchased. The necessary information comes from the pharmaceutical research department, the production men, the purchasing agents and, possibly, from others.

Having decided on the specifications and obtained at least one reliable supplier, it becomes necessary to devise tests to determine that each lot of material received meets these specifications. We need constantly to remind ourselves that it is easy to write rigid specifications that result in buying higher priced material than is necessary. This results in high-priced final products.

The next phase is control of formulas. The master formula, by which the raw materials become a final product, is



Dr. George O. Sharp has been in charge of the analytical and control department of the Wm. S. Merrell Company for 13 years. Before joining Merrell, he spent 10 years teaching and four years with the American Medical Association Chemical Laboratory. Dr. Sharp had his early education at Pittsburg, Kansas, received his AB degree from Kansas State College, his BS degree from Ottawa University in Kansas, his MS degree from Kansas State University and his PhD from the State University of Iowa.



Analyses at every stage of manufacture.

usually issued by the control department. This formula should reflect the best experiences of the pharmaceutical research and the production departments. It must be clear and concise and give sufficient details to permit the production men to produce an excellent product within the minimum time. Time wasted in producing a product or in producing an inferior product is expensive and ultimately raises the cost to the consumer.

After the batch of product is produced, the control department takes a final look at the formula and product. Does the formula accurately reflect a complete history of the batch? Are the identifying numbers and weights of all raw materials recorded, as well as the initials of the persons weighing and checking these; are any deviations in manufacture recorded; are the yields of product recorded and reasonable? Are the results of the chemical analysis within set specifications; are the physical properties of color, taste, odor, viscosity, hardness, size of tablets, satisfactory? These records, if properly kept, can be important legal documents.

Control checks for proper preparation of the packaging operation, that the batch has been okayed, that the proper container, cap, seal, stuffing, etc., are used according to definite specifications. In this operation probably the most important part is the label on the package.

Some member of the control department should be on the label development committee. In this way, control becomes aware of the legal requirements of labeling particularly in the general requirements of not being misleading. Further, it should be informative to the pharmacist, the doctor and the patient if it is an over-the-counter item. Once the label is produced it is usually control's job to check that the label and the batch being packaged agree. This is particularly important when a product is being changed and necessitates a change in label.

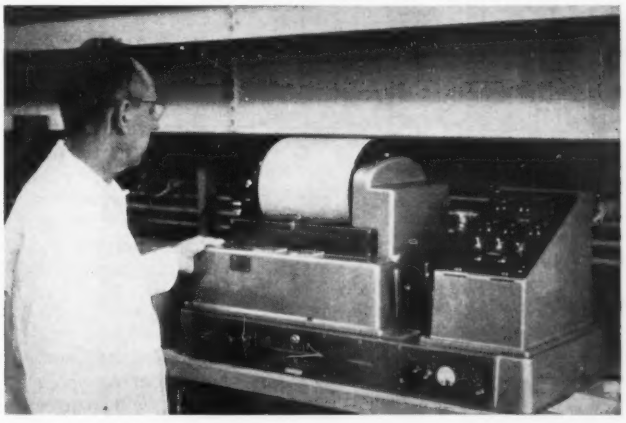
In many cases control does not perform the operation but checks to see that the operation is properly performed. A production group may prepare the label up to final copy, but control will check to see if the label is correct before the plate and electros are made.

Space will not permit us to delve into the legal aspect of our operations. Control should be aware of these requirements and potential violations. Few industries are more carefully regulated by federal and state regulations than the pharmaceutical industry. Particularly important is the Federal Food, Drug and Cosmetic Act of 1938 and the numerous regulations issued under that act. Although good business and high moral responsibility almost demand an old established firm adhere to the principles of the Federal Food, Drug and Cosmetic Act, not everyone does. Only recently an injunction was issued against a drug firm outlining certain actions required of it before it could re-enter interstate business.

We have indicated to some extent the minimum requirements of good control. There are many other things a control department does. It helps investigate complaints on a product. This may turn up areas of research for product improvement, may even turn up a batch of material that should be recalled from the market or suggest it should be withheld from further shipping. Certifications of antibiotics may be done in a control department. A large part of a new drug application for a drug is control data and information. If the pharmaceutical company does business in other countries, control may prepare data for the registration of a product, its partial or complete manufacture under quite different conditions and regulations than in the United States. For example, saccharin in Mexico is subject to special regulations and an inspector must be called when it is used in manufacturing. Saccharin in Italy is used as a check, for tax purposes, on the amount of business that a pharmaceutical company does.

Control realizes a pharmaceutical company is made up of people and people can make mistakes. Hence, checking and rechecking is essential and must be done efficiently No dangerously misformulated product must reach the consumer. One bottle with a wrong label can be very dangerous.

To do his job the control man must have co-operation with other people in the company. For the company's products and reputation he is a watchdog.



Instrumental methods—rapid and accurate control.

changing times——

*their challenge to the health professions**

by Francis H. Horn

CHANGES in contemporary society and the world that have implications for the health professions, changes that challenge all those concerned with the nation's health, pose some particularly important questions for the profession of pharmacy.

Medical and pharmaceutical science has made remarkable progress in recent years. Consider the advances in preventive medicine, for example, highlighted in our day by the discovery of the Salk vaccine for polio. Or the remarkable development of antibiotics, with several hundred such drugs today whereas less than 20 years ago there was only penicillin. Or the achievements in surgery, by which delicate operations undreamed of a generation ago have been successfully performed. Remarkable, however, as the progress thus far has been in alleviating pain, stamping out disease, and prolonging human life, still more remarkable achievements lie ahead. Before long doctors and scientists will discover how to lick the last of our great killers—diseases of the heart and blood vessels, cancer, arthritis and rheumatism, and diseases of the nervous system. The rarer, but not less deadly diseases, will also be overcome.

It is imperative, of course, that if these diseases are to be conquered, there must be continuing research of considerable magnitude. Fortunately, the federal government is now giving substantial financial support to research in the health fields. In a dozen years the annual appropriation for the National Institutes of Health has risen from 3-1/2 to 241 million dollars. But still more support is needed. With increased federal support and with support by voluntary health agencies and the pharmaceutical industry, continuing at least at its present level, it is certain that the future will see more and more research in the health fields, with comparable benefits to mankind.

The results of past health research are everywhere evident. It is clear that the advances medicine and pharmacy have made have resulted in greater preservation of life at all levels, from infancy to old age. Two of the major characteristics of our rapidly changing times are the longer life span and the rapidly expanding population. The average life span in the last half century has grown from 48 to 67 years for men, from 51 to 73 years for women. This will continue to rise. In the space of a generation, it may become quite normal to live to be a hundred.

Lowered mortality and living longer have combined with an increasing birth rate to produce substantial population growth. It is difficult to know what future population will be, since the demographers are always revising their estimates upwards. Recent predictions forecast a population in the United States of more than 225,000,000 by 1975. Today it is 175,000,000.

changes create problems

These changes in our society resulting from constantly improving health services pose significant challenges.

☞ **First** is the fact that we shall have substantially greater proportions of our population who are children and who are past the biblical span of three score years and ten. The major problem, healthwise, is with the aging and aged. Increasingly our senior citizens will be in possession of their mental and physical powers, but eventually deterioration must set in. With their numbers increasing so rapidly and their life being prolonged into the 80's, the 90's and even over the century mark, the problems of providing health care are multiplying. Special problems will exist for the pharmacist, for all sorts of drugs will be offered to the elderly and old—some beneficial, some harmless, some downright dangerous. The pharmacist will face both professional and ethical problems as he attempts to serve the legitimate drug needs of an increasingly elderly population.

☞ **Second,** not only the older elements of our population, but all age levels, will require more medical attention and expanded health services. We have been increasingly conditioned to the necessity of "seeing the doctor." Many a mother rushes her child to the physician when he has the sniffles; a generation ago, she would have done her own doctoring. From car cards and billboards, magazine and newspaper advertisements, radio and TV announcements, we are warned that if cancer doesn't get us, heart disease will and we are urged to see our physician. New wonder drugs are forced on our attention with greater insistence than ever before. Immunization of all kinds is standard procedure for most families. Nowadays, children cannot go to school or college, to camp, or travel without first getting numerous shots. Hospital and medical service coverage is carried increasingly by regularly employed persons and is a fringe benefit for more and more of them. Insurance against major medical disasters is becoming more common.

At no time in history—and possibly in no other country—have people been so health conscious, in the sense of requiring the ministrations of members of the health professions. Consequently, demands on the pharmacist are increasing proportionately, perhaps even more than the increased demands for all health services. The more medical service rendered, the more drug service required. But the pharmacist also faces the growing problem of self-treatment. Thousands of new drugs are on the market, most of them advertised extensively. Though Father John's, Lydia Pinkham's and Carter's Little Liver Pills are still on the shelves, the competition in drugs is fiercer than ever and the pharmacist will be called on increasingly to appraise the relative merits of these numerous drugs and to recommend the proper ones to the inquiring customers.

Let no one suggest that the present-day pharmacist, dispensing ice cream, greeting cards and miscellaneous sundries and hardware in the modern chrome-plated drugstore, is only a merchandiser with no greater responsibility than if he dispensed only such items. More than ever he is an important member of the health profes-

* Address given at the annual meeting of the Rhode Island Pharmaceutical Association and Traveling Men's Auxiliary, June 23, 1959.

sion because, while less and less of his work will be devoted to compounding drugs to fill prescriptions, he will be dispensing more drugs—pre-packaged, it is true—than ever. The answer to "What vitamins should I take?" places somewhat more responsibility on the pharmacist than recommending one brand of aspirin over another. The druggist of the future will be more of a pharmacist, not less, than in the past. In the future, it is obvious, despite continual progress in medical care and treatment, the demand for health services of all kinds will constantly expand.

☞ **Third,** to serve the health needs of an ever-enlarging population, persuaded by all the technic of modern advertising of the importance of health care, will require tremendous increases in health personnel and facilities. One of the major challenges of the future will be providing adequate numbers of physicians, surgeons, psychiatrists, dentists, nurses, pharmacists, dietitians, physical therapists, medical and dental technicians and the other specialists concerned with the maintenance and improvement of health. Providing the required number of research scientists for the laboratories in the health fields and of specialized teaching personnel for the schools and colleges in these fields will likewise be a major problem. Similarly, there will be a real problem in providing the required clinical, laboratory, and hospital facilities, both for health service and for professional preparation of practitioners.

☞ **Fourth,** answers will also have to be found to the problem of the costs of health services—both to the individual and to society. The matter is acute in terms of the charges for medical service; the cost of drugs is also a matter of increasing concern. President Eisenhower recently appealed to the national convention of the American Medical Society to hold the line on fees. The other aspect of this problem is the cost of health services to society. Medical treatment is more and more expensive. Institutionalized care is seldom covered by the payments of the patient, high as these are. In addition, with an increasing load of welfare cases of one sort or another, the drain on the fiscal resources of local communities and states is staggering. Some means of meeting the problem must be found.

changes pose challenges

The discussion thus far has concerned some of the problems that individuals, the health professions and government are facing because of the extraordinary success of the health sciences. It is paradoxical that the more successful these sciences are in overcoming disease, the greater the demand for health services becomes. It is also true that despite the remarkable progress in health services which has resulted in improving the health of the nation, changes occurring in our day—and the still greater changes that will come in the future—may well offset the advances that have been made in overcoming pain and combating disease.

Modern technology has produced a new tempo of life. For one thing, life has speeded up. Autos, boats, airplanes—all go faster and faster. Air speeds of as much as 5000 miles per hour are being predicted. We are studying the physiological effects of these increased speeds. They may produce new health problems, we do not know yet. But of one thing we can be pretty certain. Higher speeds, along with vastly increased numbers of vehicles as the population expands and our higher standard of living permits more vehicles per family, will result in more accidents, many fatal, of course, but most resulting in injury of one sort or another. Consider the potential for accidents when vastly larger numbers of people learn to fly and operate their own airplanes. *The medical profession may well lick the last major diseases, but it will surely face new and growing challenges in the areas of physical rehabilitation and plastic surgery.*

New challenges to health will likewise result from man's probing the depths of the sea and the outer reaches of space. Improved technology, especially the spread of automation, will create new health problems for large numbers of people. There will be less physical fatigue, but other kinds of fatigue will become more widespread. The almost constant noise in which individuals live certainly contributes to mental fatigue. The increase in leisure and the inability of many to know how to enjoy it may create or aggravate health problems. Intensification of weekend athletics and recreation for those not in good condition for such activities will certainly add to the amount of health problems, though it may not create any new ones.

Certain other conditions of modern life contribute to the challenge to health. There are the often overpowering uncertainities of existence with the consequent search for security. With one out of three marriages ending in separation or divorce, broken homes add to contemporary health problems. The cold war and the threat of annihilation contribute to the general uncertainty, above all to a prevailing sense that man no longer has any control over his destiny, that he is prey of forces over which he has no control.

These and similar conditions of our times—and the future seems to promise their aggravation—produce all sorts of

Born in Toledo Ohio, Dr. Francis H. Horn, president of the University of Rhode Island, has had a career that has practically spanned the globe. It has included teaching at the American University at Cairo, Egypt, serving four years in the Army for which his last assignment was as assistant dean of Biarritz American University in France, being dean of the Junior College of Commerce in New Haven, associate professor of education at Johns Hopkins University, executive secretary of the Association for Higher Education in Washington, D.C., president of Pratt Institute in Brooklyn and visiting professor at Southern Illinois University.

tensions and frustrations, resulting in psychosomatic troubles, alcoholism, nervous breakdowns, and suicide. Mental illness accounts for about half of our hospital cases. But many people with mental troubles never reach the hospital. More and more individuals depend on drugs to get them through the day. Some need "pep pills," others, tranquilizers. It is not uncommon for the same person to need an energizer to get going in the morning and a sleeping pill to get to rest at night. With few exceptions, those usually involving violation of the law, such pills are dispensed by drugstores. The increasing use of such drugs presents a special challenge to the pharmacist and subjects him to pressures sometimes hard to resist. But resist them he must. In any case, *meeting the problems of mental disease may well be the major challenge to health as we enter the new age that lies ahead of us.*

The age is creating other conditions which challenge health and increase health problems. Many spring from scientific research and technological progress. There is, of course, the ever-present danger of another world war, with the possibility of mankind's annihilation. Even if mankind were to survive a modern war, the problem of restoring the survivors to health would be staggering. I am optimistic and do not expect such a war to develop; but *preparation for the eventuality of war is currently challenging the health advances*

man has made over the years. The problem of radioactive fallout from the testing of nuclear weapons is certainly the most serious—and most controversial—of the health problems. Atomic waste and its disposal is another which, as peacetime uses of atomic energy increase, becomes more acute.

In another area, that of nutrition, science is making discoveries that may challenge health with new sources of food and new methods of food processing. Chemistry is being used increasingly to modify the nature of the things we eat, through both what it removes and what it adds to food. Who knows what may eventually result from the continued application of science to food? For years we have joked about eating only pills. In time, the drugstore may replace the restaurant and the family kitchen as the source of our meals.

Likewise, *scientific experimentation*—some would call it tampering—*in other areas may produce new challenges to health.* There is the matter of weather and climate control. Artificial semination in humans, now practiced on a limited scale, could lead to controlled breeding of humans, just as it now does of racehorses. We may live to see the day when the pharmacist dispenses, upon prescription, the means to propagate the race just as he now dispenses, without prescription, the means to prevent such propagation.

Other possibilities of manipulation of "normal" or "natural" processes will develop in the future. Greater control of the individual environmental factors of life seems inevitable. Any increase in this matter has implications for health and those in the professions.

Also important in challenging health in the future are certain cultural and sociological environmental factors. One is the increasing percentage of married women in the labor forces. Some 60 per cent of working women also are responsible for homes. Another is the greater mobility of our people. One out of every three families moves every two years. There are also health problems, more serious than just the sanitary ones, in the increasing number of people who live in "mobile homes." The number of Americans living abroad, often in Asia and Africa, is growing rapidly. Including the military, there are now over two million. The health conditions some of them face pose new problems.

One environmental factor that has a major challenge to those in the health fields is the growing urbanization of the country. There is still some doubt whether the process will result in further deterioration of our cities or provide the incentive to make them healthier and happier places in which to live and work. The race is still between creeping slums and urban renewal. We have the technical know-how to win the race; whether we have the will to do so and are ready to pay the cost remains to be seen.

challenge to pharmaceutical education

What does all this mean in terms of the education of a pharmacist?

☞ **First,** the need for good health is greater than ever before. The need for robust physical health may not be so great as it was when we were carving a new nation out of the wilderness or pushing the frontier across the continent, but never before was good health in all its aspects so important. In these precarious and uncertain times, in which, indeed, the future of mankind hangs in the balance, with life speeded up on every hand so that critical decisions often have to be made in a split second, and with the increasing complexity of the problems facing a shrinking world, the individual requires sound health. We must have cool heads and our emotions under control, difficult indeed if the individual does not enjoy good mental and physical health. The old Greek ideal of a "sound mind in a sound body" is even more relevant for our time.

☞ **Second,** to help produce this ideal more widely, we need a more effective program of health education in our schools and colleges. It is essential in creating the conditions in today's and tomorrow's society by which the individual can live a healthier, and consequently, happier and more satisfying life. The proper use of drugs, their place in maintaining and improving health, is surely an integral part of such health education, although one sadly neglected in current programs. Greater co-operation is needed on the part of educators and the health professions if the most effective results are to be realized.

☞ **Third,** There is a critical shortage of people in the health professions. The universities are not turning out enough graduates in these fields even to keep pace with the increasing population, let alone with the growing demand for health services. Means must be found to stimulate more young people to prepare for service in the health fields. And with the increasingly complex problems that those on the health team must face, professional training must be constantly improved. At the same time, it should be obvious that specialized training is not enough. The worker in the health fields requires an increasingly broad background of knowledge bearing upon both the individual and collective environment. The health professions have recognized this and are stressing the importance of liberal education accompanying the scientific and professional training. With knowledge of all kinds expanding so rapidly, it will become increasingly difficult to provide the necessary education and training in the years that can be given to it in school and college. But constant study by colleges and universities and practitioners as to how it can best be done is a must if we are to provide the members of the health professions needed by our changing society.

In addition, it should be clear, continuing education, of both a general and professional nature, is imperative for such practitioners. Colleges and universities should work more closely with the professions in providing opportunities for appropriate continuing education.

As with the other health professions, pharmacy education over the years has been lengthened in time and improved in quality. Only 55 years ago standards for admission to colleges of pharmacy were set at a "common school education entitling the student to enter high school." Four years later, it was raised to one year of high school; it was not until 1923 that a high school diploma was required for admission. In 1932, the four-year pharmacy curriculum was adopted. And now, beginning in 1960, it will be increased to five years. The Blauch-Webster report for the committee on curriculum of the American Association of Colleges of Pharmacy, published in 1952, actually recommended a six-year curriculum, a four-year professional pharmacy curriculum on a two-year general education base. This recommendation was not adopted, and approval of the five-year curriculum was obtained only over determined opposition.

If the outline I have presented of the health problems of the future is a valid one, then it seems obvious to me that the five-year curriculum is the minimum that should be expected for the education of a pharmacist. The pharmacist who expects to go into the corner drugstore plays an increasingly important role in meeting the health problems of the nation and, with the rapid expansion of knowledge in the pharmaceutical field, he must have a thorough professional education.

A decade ago, the committee on the pharmaceutical survey expressed the objectives of pharmacy education:

> **The pharmacist must be a professional man who understands thoroughly what he is doing, who comprehends the scientific bases of drugs and drug actions, who is able to evaluate critically the products he handles, who is competent to advise physicians and members of the other health professions concerning drugs and their uses, who works at his profession creatively and advances its service.**

Professional knowledge of drugs, however, and of the advances in medical science, is not enough.

If the pharmacist is to work at his profession creatively, he, like his brothers in medicine and dentistry, must have some knowledge about society and the environment in which human beings live. It is not enough that the pharmacist understands the basic physical and biological sciences; he must also have some acquaintanceship with the social sciences and the humanities. These studies are professionally essential to the pharmacist in the light of the changing world of today and tomorrow. They are also personally essential, for the pharmacist is a citizen and an individual. Such studies, as the Blauch and Webster volume state, help to build up the "intellectual and moral resources which contribute to the enrichment and enjoyment of personal living."

The pharmacist, as a matter of fact, perhaps has more need of broad knowledge, of good psychology, of human understanding, than the doctor or dentist because he sees most of his customers far more often than the healers see their patients. Few professions offer the opportunity that pharmacy does to be counselor and friend to so many people of all ages. But the job demands more education than it has ever required in the past.

Pharmacy is a great profession above all because of the opportunities it provides for service to mankind. The changes our society and the world are undergoing make the challenge to dedicated service greater than ever before. ■

FIP council meets in Madrid

PHARMACEUTICAL representatives of more than 30 nations met in Madrid, Spain, September 14–18 for the meeting of the Council of the International Pharmaceutical Federation. In opening the meeting, President Sir Hugh Linstead warmly thanked the representatives of the Spanish Pharmaceutical Association for the splendid reception they had given the FIP, for the many special events they had planned, and, especially, for providing for simultaneous translations of all discussions into English, French, German and Spanish.

So that representatives of the various national associations could be informed as early as possible of items to be discussed and voted upon, the council adopted a new order of procedure for the general assemblies of the FIP.

Reporting for the Scientific Section, Professor Ruyssen (Belgium) discussed the highly successful International Congress of Pharmaceutical Sciences held in Zurich September 6–11 in which more than 500 pharmacists participated. He pointed out that the Scientific Section's three main objectives are to establish unity in pharmacy, to encourage research and to hold international congresses of pharmacy. Professor Ruyssen told of plans to hold a symposium on pharmaceutical education in Copenhagen in 1960 during the meeting of FIP, in addition to the regular features of the Scientific Section.

President Franz Linner (Austria) of the Section of Hospital Pharmacists reported on the Congress of Hospital Pharmacists held in Vienna in June with more than 140 in attendance. Speaking of plans for the meeting of the hospital pharmacists in Copenhagen, President Linner mentioned that he hoped to arrange one meeting of the section in Stockholm, probably just prior to the congress in Copenhagen.

Dr. Don E. Francke, president of the Commission on Pharmaceutical Abstracts, reported results of the commission's meeting in Berne, September 3–4. The commission decided that a pharmaceutical abstract service is necessary and moved toward establishing an abstract journal which would be published fortnightly in English with titles in the original language, also, contain 80 pages with abstracts printed on one side of the page for easy cutting, and contain approximately 6,000 abstracts per year, having an average length of 200 words each. Following his report, the council voted 200 pounds sterling to carry on the work of the commission.

Dr. J.H.M. Winters, secretary-general of the FIP, was appointed editor of the *Journal Mondiale de Pharmacie*. In taking over this post, he succeeds Dr. Paul Degand who recently resigned.

Plans for future FIP congresses were approved as follows: *FIP general assembly*, August 28–September 2, 1960 in Copenhagen; *International Congress of Pharmaceutical Sciences*, September 4–8, 1961, in Pisa, Italy; meeting of *FIP council and bureau*, September 11–15, 1961, in Athens, Greece; *FIP general assembly*, September 1962, Vienna, Austria.

During the meeting President Linstead spoke of some of the problems of FIP and of pharmacy in general, and requested future discussion by the council on some of the challenges facing the profession. In pointing these out, Sir Hugh said,

> **Pharmacy has its own field of knowledge and its own standards of conduct and practice. Decisions upon pharmaceutical problems can be properly taken only by pharmacists. That is the essence of the indepencence of pharmacy. Pharmacy is indivisible in the sense that the science, the industry and the profession are complementary. The training of students and academic research have no meaning if they are divorced from practice. Equally, if pharmacy ceases to be scientific it loses the reason for its existence. Nor, in this century of internationalism and the WHO can pharmacy in any country insulate itself from pharmacy elsewhere. Finally, pharmacy must have integrity in the sense that it must accept complete responsibility for the medicaments it prepares and supplies.**

an historical symposium

innovations in dosage forms . . .

the story of

lozenges

by H.W. Moeller

THE USE of lozenges as a method for administering medication dates back to 500 B.C. At first, the medicinal discs were called "troches," meaning circular or round. As time went on they were called "pastiles" in Latin and finally "lozenges" in English.

Lozenges were made by rubbing dry medicaments with vinegar or wine. The material was rolled into the form of a cylinder and then cut into discs. Later mucilage, juices and syrups were substituted for wine and vinegar.

One of the most famous early lozenges was composed of goats' blood and earth from the Island of Lemnos. The earth was excavated at a ceremony held yearly on May 6. It was transported to a nearby village where it was washed, dried and mixed with goats' blood and then rolled to the proper thickness. The roll was then cut into lozenges and imprinted with a seal. The earliest seal was in the form of a goat. Also used were the head of the goddess, Diana; the likeness of Christ; and the Turkish half-moon.

During the middle ages a large variety of lozenge presses were used. The Islamic mold dating about 1400 A.D., preserved in the museum at Istanbul, Turkey, is one of these and is quite elaborate. The lozenges made from this mold have the inscription, "In the Name of Allah, the Merciful, the Compassionate." Many presses such as these, with various inscriptions or figures, are on display in museums throughout the world.

Equipment for rolling and cutting lozenges including a wooden rolling board, a roller and a cutting punch was described by Edward Parrish in 1856. Within the next 20 years, at least a dozen such machines were patented in the United States.

In Remington's *Practice of Pharmacy* is a description and illustration of an adjustable lozenge board which was introduced by F. L. Slocum in 1879. A variety of shapes and sizes of punches was introduced in the ensuing years for the manufacture of lozenges.

Harry W. Moeller, manager of production processing and engineering in the development department of the William S. Merrell Company, has been associated with the firm for 21 years. His posts have included those of bacteriologist, analytical chemist, analytical and control department head and production manager. He holds a degree in chemical engineering from the University of Cincinnati, is secretary of the Cincinnati chapter of Society for Advancement of Management and is president of the Finneytown Board of Education.

The *U.S.P. VII*, issued in 1890, gives the following description for the preparation of lozenges:

> Powders are mixed together and a mass is formed with water. The mass is then divided into troches or lozenges.

In checking a Merrell catalogue of 1894, I noted that there were 45 different lozenges listed. Some of the more interesting ones were capsicum, cinnamon, cloves, licorice, musk, peppermint, rose, sassafras, wintergreen, potassium chlorate, pepsin, ipecac and pine tar with ammonium chloride. These have practically all fallen by the wayside.

Today most lozenges are made in one of two ways—either in the form of a compressed tablet or with a hard candy base.

The compressed tablet type is made in the same manner as any other tablet.

Briefly, the method of manufacturing is as follows:

The dry ingredients are placed in a mixer and the liquid granulating material and color are added. The materials are thoroughly mixed, removed from the mixer and ground through an oscillating granulator. The material is then spread on trays to dry and reground to a finer mesh size. The material is then returned to a mixer, usually of the tumbling type, and lubricated. After being lubricated, it is transferred to a compressing machine and compressed into lozenges at speeds up to 4000 revolutions per minute. These are usually packaged into bottles, boxes or strips.

The one difference between a lozenge and a compressed tablet is that the base of a lozenge is usually sugar while that of a tablet may or may not be sugar. According to the original definition of the word "lozenge," the compressed type is not, in the strict sense of the word, a "lozenge."

This paper and the five which follow were presented before the section on historical pharmacy of the AMERICAN PHARMACEUTICAL ASSOCIATION *in Cincinnati, Ohio, August 19, 1959.*

The hard candy-type lozenge fits the definition more closely since the soft candy mass is extruded into the form of a rope and is compressed while soft into a lozenge. Merrell's Cepacol lozenges are produced in this manner in a continuous operation.

Briefly, the operation is as follows:

Sugar, water and glucose are fed automatically to a continuous dissolver. The material is heated and transferred automatically to a cooker where a vacuum is drawn to remove the water. The mass is then transferred to a kneading machine where the active ingredients are incorporated. Following this operation, it is transferred to a large rotating hopper where the candy is extruded through a series of rolls to form a rope. The rope is fed into a forming machine where the individual lozenge is formed from the plastic material at a rate of 2600 pieces per minute. The hot, soft lozenge is then transported onto a three-tier cooler in a special air-conditioned room. After cooling, the lozenges are automatically inspected for size and then visually inspected in a single layer on a moving conveyor belt. They are then heat-sealed in a protective foil strip on automatic machines. The packaged strips are placed in a bucket conveyor, transported to a cartoning machine and then to a cellophane wrapper.

The cellophane-wrapped cartons are automatically stacked and placed in a display packer, which in turn, are placed in corrugated cases, and carried by belt conveyor to the warehouse, where they are stacked on pallets ready for shipment.

From the foregoing, it is apparent that lozenges were made in about the same manner from 500 B.C. to almost the beginning of the 20th century.

In the last 50 years—and more specifically in the last 25—great advances have been made in production methods and, undoubtedly, one of our modern machines produces more lozenges in a day than one man could produce in a lifetime back in 500 B.C. ■

Lozenge manufacture at The Wm. S. Merrell Company

friable pills and escaps

by D.T. Meredith

ALMOST three quarters of a century of pharmaceutical progress separate the two dosage forms, Friable Pills and Escaps,* both products of Upjohn. Friable Pills, a name synonymous with the company for the first 25 years of its history, represent a product of the 19th century—a product which has almost outlived its usefulness. Escaps (electron sterilized capsules), definitely a product of the 20th century and the age of electronics, lived scarcely long enough to prove their usefulness. Yet both were pharmaceutical innovations.

'friable pill'

The Friable Pill was a dosage form designed to overcome certain shortcomings of the mass pills of the 19th century, primarily problems of disintegration and variable dosage. They were produced by a process which involved applying successive layers of medicinal ingredients to "pill starters" revolving in a specially designed "pill tub."

The pill tub used in this process resembled a coating pan used to coat tablets in modern pharmaceutical manufacturing with one exception—it was constructed mainly of wood rather than of all metal. In fact, the process of manufacturing Friable Pills resembled closely the present day process of coating tablets.

Additional equipment used included measuring sticks and sizing screens. The measuring stick, used in sizing pills, is a "right-angled trough" closed at one end. Constructed of wood, it has indentations for fifty pills on one side and a graduated measuring scale on the other. The stick was dipped into the pills and the indentations picked up 50; the stick was tilted and the 50 pills measured on the graduated scale giving the pill size. Fifty pills measuring 12 inches were known as "12-inch pills," etc. If the pills were smaller than standard for any particular formula, they could be built up by further applications of inert material.

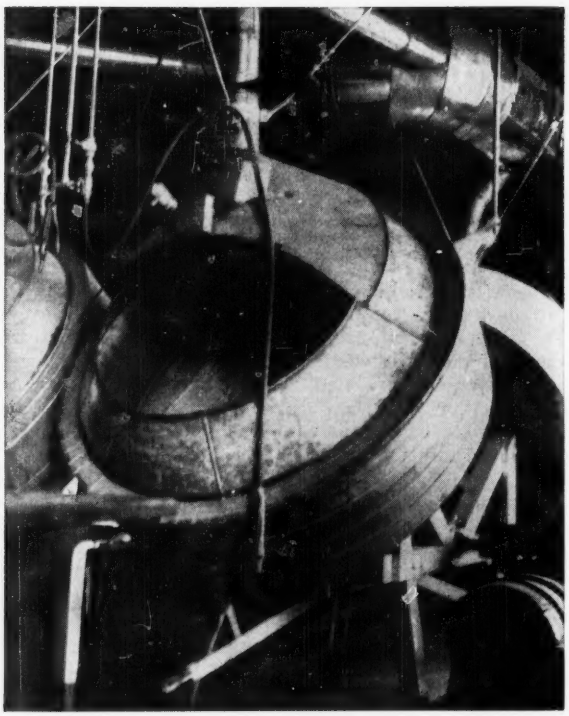
Made of sheet metal, usually zinc, the screens were accurately perforated to the thousandth of an inch and rolled into cylinders. They were gear driven for rotation. Pills entered from a hopper at one end and fell into trays at the other end. While turning, the screen was sharply rapped twice during each revolution to prevent the pills from clogging the openings. The desired size flowed out of the end and the small "drop-through" fell into receptacles under the revolving screen, and were returned to the tub for additional applications of "pill stock." To be accurately sized, the pills had to pass over one mesh screen but fall through the next larger-sized mesh screen.

A most important part of this opera-

* *Trademark, Reg. U.S. Pat. Off.*

tion was the preparation of starters. These were made by placing about ten pounds of granulated sugar of 50-mesh size in a rotating pill tub. The granules were sprayed with a mist of water until the sugar was evenly moistened. A powder composed of talcum and sugar was then dusted on the damp material until the mixture felt or appeared to be partially dry. Alternate applications of water and the dusting powder were added until small globules were formed. By alternately screening, then moistening and dusting, the starters were built up to the correct screen size. Several hundred pounds of starters were produced from ten pounds of sugar.

The process of making pills was the same as that of making the starters except that the nucleus of the pill was the little sugar starter. The fluid excipients were usually water or oil and in some cases both. Properties characteristic of the drugs and mixtures used in the pill determined which excipient should be used. Hygroscopic, resinous extracts and freely soluble materials required oil; water was used for less soluble and insoluble materials. Oil was applied by dripping on the pills in the rotating tub; water was sprayed in the form of a mist as mentioned in the discussion of starters. The process again involved alternately moistening and sifting on ingredients and sizing through screens until the entire stock of ingredients was used up and the pills were of a uniform size. They then were coated to preserve size and shape in regular coating pans as are used for tablets.



A pill tub used by the Upjohn Company to manufacture "friable pills." Unlike the coating pan, the pill tub was constructed mainly of wood rather than of all metal.

Don Meredith, a native of Brook, Indiana, served a two-year pharmacy apprenticeship in the drug store in his hometown before going on to Purdue University to earn his PhD degree in 1931. His career has included being a registered pharmacist, a pharmaceutical salesman, a graduate assistant in the Purdue pharmacy school while earning his BS and MS degrees in pharmacy, instructor at the Detroit Institute of Technology, college of pharmacy, and an inspector for the Army Medical Purchasing Office. In February 1946 he joined the Upjohn Company and has risen from a salesman to his post as head of the trade and guest relations department. Meredith is a member of Kappa Psi, Sigma XI, Michigan Academy of Pharmacy (past president), American Pharmaceutical Association and APhA Michigan Branch (past president).

"escap"

Escap was a dosage form designed to provide a means of supplying sterile ophthalmic ointments in a single dose applicator container.

The ointment was prepared in the usual manner and then encapsulated on a special adaptation of the Colton soft capsule machine. This machine actually consists of two units, a casting machine and a hydraulic press. Gelatin which has been mixed with water and melted to the proper consistency is fed into the casting machine from a temperature-controlled holding tank. It first passes into a spreader box then feeds at a regulated thickness in the form of a ribbon over a series of temperature-controlled revolving drums. This unit, then, forms a gelatin ribbon, cools it to the proper temperature for the final molding process, and cuts it into sheets of the proper size by means of a revolving knife.

The gelatin sheet is next laid over the lower mold plate which is part of the hydraulic press. The sheet, by the way, is twice the size of the plate. A vacuum line is attached to the plate and this forces the gelatin into the individual molds. The fill is accomplished through a set of little piston pumps which deliver the exact measured amount to each of the individual molds as the plate moves under the filler head. The operator then folds the remaining half of the gelatin sheet over the lower plate, drops the top plate into position, and the mold is carried into the press. The press forces the two mold plates together, sealing the capsules and cutting them out, leaving a gel net. They are then ready for washing, packaging and sterilizing.

The real innovation in this process, of course, was the sterilization of the capsules. Sterilization was accomplished by placing previously cellophane-packaged Escaps on trays which were in turn placed on a conveyor belt. The conveyor belt carried trays of Escaps to a Van de Graaff accelerator for electron or "cold" sterilization. The Escaps passed through a beam of electrons which, traveling at a speed of about 175,000 miles per second, penetrated the cellophane-packaged Escaps and killed any bacteria present. The same conveyor then carried the sterilized Escaps to a window where the trays were unloaded and subsequently moved back to the packaging department for boxing and labeling.

This product is not currently being marketed. It was market tested on a limited basis but it did not receive wide enough acceptance for general release.

the gelatin capsule

by L.B. Stadler

ALMOST everyone has seen Adriaen Brouwer's picture, entitled, "Bitter Medicine." This picture graphically epitomizes the need for a suitable means of disguising the taste of dry medicines and dramatizes the pharmacist's long search for a dosage form that would solve this vexing problem. Of the many devices tried—most of which were soon cast aside—the empty gelatin capsule and the coated compressed tablet have best stood the tests of time and experience.

The term, "empty gelatin capsule," refers to a two-piece, hard, gelatin, telescoping capsule. The Romans had a word for it; in fact, they had two words, one developed from the other. "Capsa" is the Latin word meaning case. From this developed the diminutive, "capsula" meaning a small case.[1] An advertising definition employed in the late 1870's describes capsules as "two small tubes of prepared gelatin, one sliding into the other, and each closed at one end. The remedy employed is then separated into the proper dosage, one of which is placed in the smaller tube, which is then telescoped into the larger. It is now in the shape of a small cylinder . . . closed at both ends." This early description goes on to state that "the gelatin on being moistened becomes slippery and is readily swallowed with the aid of a little water."[2]

Empty gelatin capsules have come to be looked upon as the most versatile, many-use medicinal container. They are unique, being one of the packaging units where both the container and its content are simultaneously swallowed for convenience in administration and accuracy of individual dosage.[1]

Forerunners of today's empty gelatin capsules were first prepared in a very crude form by A. Mothes, a French pharmacist, in 1833. Report of his discovery was made to the Académie Royale de Médecine, in May, 1834.[5] Capsules were first made in the United States by H. Planten in 1834 or 1835, but they were not recognized as being particularly valuable. No perceptible advance was made in their manufacture for many years.[2] The first two-part telescoping capsules were made in the United States in 1863, but their usefulness was impaired by the poor fit.[5]

One of the first inventors to design machinery for the manufacture of empty gelatin capsules was F.A. Hubel of Detroit, Michigan. Inspired by reports from Italy in 1874, Hubel, a retail pharmacist, first made molds of iron wire mounted in blocks of wood. The capsules were trimmed with a penknife. He made pins of different diameters for body and cap.[5]

The first capsules listed in the Parke, Davis catalog in 1875 consisted of three sizes that are now known as Nos. 1, 2, and 3. They were still rather crude, but an attempt was made to give them a smooth and transparent appearance and to produce a body with cap slightly larger so that they would properly fit together.

Capsule manufacture got its first big boost after 1875—when aggressive sales and promotional efforts were put behind them. Capsules were first made in quantity by Hubel, but there soon were several small competing firms in the business of making capsules for other companies to sell or for their own sales organizations. One of those active in the field was James Wilkie, who first became interested as a salesman supplying the carefully-gauged iron wire used for molds. Wilkie is credited with having introduced phosphor-bronze wire for molds—a product superior to iron which remained in use until replaced by stainless steel in the 1930's. Wilkie was interested in the U.S. Capsule Company, which consolidated a number of competing firms, and, for a time, supplied most of its product to Parke, Davis.

About 1901, this firm and its subsidiary, M.L. Capsule Company, were purchased by Parke, Davis. Then began an expansion and improvement of manufacturing processes under the supervision of James Wilkie. Capsule manufacturing received its greatest stimulus, however, in the 1920's, when automatic filling devices were perfected.

Many of the mechanical improvements in manufacturing pharmacy came from the ideas and inventions, most mothered by necessity, of the men who were charged with the operation of the machines. Thus there grew up not only a corps of chemical engineers but also a class of pharmaceutical engineers, highly versatile and capable of performing near miracles of production from the equipment they designed. In the 1890's, for example, it was visualized that manufacture of empty gelatin capsules might some day reach the staggering production peak of one million capsules a year. Sixty years later, production of one million capsules occupied hardly more than an hour's time in a well-ordered division of a pharmaceutical manufacturing plant. Even today, certain specialized machining operations are performed in the capsule department's own engineering and machine shop.

Today the interest in capsules is greater than at any previous time. This interest is not a mere fad but shows a direct relationship to the degree of development in the mechanical art of making capsules as well as the technical progress in production of highly refined gelatin. To cite an example, in 1896, empty gelatin capsules were trimmed on a hand cutting machine, after which operation each individual capsule was joined by a hand operation. If every procedure ran smoothly, an efficient employee could produce 10,000 to 12,000 capsules per day. Today, through mechanical improvements, this operation is done automatically without the capsules being touched at any time.

The intricacy of mechanical movements and the precision timing necessary to produce a single gelatin capsule is impressive. To produce gelatin capsules, each machine sets in motion 40,000 accurate, precision-made casting molds. These polished casting molds must be oriented and then dipped into an accurately made gelatin solution. The solution is held at just the right temperature, neither a half degree too cool nor too warm. Even air of the

This is a photograph taken about 1925 showing the "Wilkie" machine for making empty gelatin capsules at Parke, Davis and Company.

Dr. Louis B. Stadler, senior analytical chemist at Parke, Davis and Company, is a loyal Michigander as a look at his record would tell. Not only is he an employee of a Michigan firm, but he is also a registered pharmacist in Michigan and a former teaching fellow at the University of Michigan. In addition he received his BS in pharmacy and his PhD in pharmaceutical chemistry from the University of Michigan.

entire surrounding room is maintained at exactly the same temperature and degree of humidity, summer and winter.

The capsule-casting mold is dipped into a specially prepared gelatin solution each time in exactly the same manner. The mold leaves the solution in precisely the same manner and is twirled in the same way in preparation for its course through the drying kilns.

As the molds carrying their dried gelatin films leave the drying kilns, they enter an automatic unit which re-orients the molds, strips off the newly made capsule sections, trims them to just the right length, places the cap section over the body section, after which a small conveyor belt carries them off to a waiting container ready for delivery to the inspection department.

Inspection is not a casual looking-over but is a careful and time-consuming operation. Each capsule is passed over an illuminated glass surface, where trained hands and eyes separate and remove the defective capsules.

Following inspection, capsules are counted, packaged and then distributed to all parts of the world. A special waterproof package is provided for capsules going to tropical climates—this insures good fitting properties and high quality upon arrival at the far off market-places. The care and precision that goes into the making of thousands of casting molds is reflected in the smooth, brilliant finish and the uniformity of the capsules. Industry has been willing to invest large sums for huge production machines, refrigeration equipment of hundreds of tons capacity and many highly specialized precision instruments for the control of the manufacturing process. This has provided the pharmaceutical industry with a high quality, precision-made empty gelatin capsule—an elegant container to overcome the taste barrier.

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pioneers of tablet-making

by Philip H. Van Itallie

THE archhistorian of tablet-making appears to have been Joseph R. Wood, who wrote a book about it in 1906. Many facts from this and later sources were assembled and presented 48 years ago before the historical section of APhA in an address at Nashville by Dr. L.F. Kebler.

The earliest record of a device for making what were then called "compressed pills" is found in an English patent issued in 1843 to William Brockedon. It consisted of a hollow die of appropriate size and shape into which the proper amount of powder to be compressed was deposited. After the powder was deposited, a hammerblow compacted it into a tablet or "pill," which was then removed.

In his patent Brockedon admitted the greater antiquity of molds for compressing clay to be subsequently baked into bricks and tiles, but he claimed priority in applying pressure to small steel molds for tableting medicinal powders.

Brockedon did a thriving business both in England and in the United States but, sometime during the 1860's, he started getting competition from an American tablet-maker named Jacob Dunton, who was also a wholesale druggist in Philadelphia. Dunton's original device went back to 1864 and remained secret until, after making further refinements in it, he obtained a patent for it in 1876. The Dunton pill machine was very similar to the earlier Brockedon punch and die device. It was also operated by a hammerblow.

In 1872, Henry Bower, a mechanic employed by Wyeth, constructed the first rotary tablet machine, probably

Philip H. Van Itallie is editor of Wyeth's publications, *Pulse of Pharmacy* and *Therapeutic Backgrounds*. From 1932 to 1945 he was technical editor of *Drug Topics* and *Drug Trade News*. Previous to that time he edited a publication for the perfume and cosmetic industries. He received his BS in chemistry from the Polytechnic Institute of Brooklyn in 1928 and his Master of Science degree from the same institution in 1942.

Drawing from an actual photograph of the Davis and Lawrence laboratories in Montreal about 1885 showing the tablet machines in operation.

first used for making tablets of potassium chlorate. It was characteristic of the times that John Wyeth and Brother relied on secrecy rather than a patent to protect its exclusive rights to this early machine. Bower's name did not appear on any official record until 1879, at which time he acquired, on behalf of Wyeth, the rights to the improved tablet-compressing machine invented by Jabez H. Gill. It is likely that this machine was a refinement of Bower's early model. The powdered drug that was to be compressed was fed automatically to a series of molds set in a rotating horizontal disc. By a cleverly arranged series of co-operating mechanisms actuated from a single drive shaft, the metal disc alternately turned and stopped. During each stationary interval, powder was placed in the mold, a plunger was brought down upon it and the pellet so formed was ejected by means of a rod. Then the disc revolved to place the next mold in the filling position.

Subsequent patents were issued, respectively, in 1881 to Gill and in 1885 to John Lusby, for machines to which Wyeth acquired rights. Their principal features appeared to be improvements in the mechanism for removing the tablets from the mold without breaking them. The quantity of powder deposited in the molds was also more carefully regulated.

There was one other early inventor of a rotary machine, a Philadelphian by the name of Dr. Joseph A. McFerran. He obtained a patent in 1874, the text of which suggests that the invention was inspired by previously existing cartridge-filling machines. Whether Dr. McFerran's machine did not work out in practice is difficult to determine at this late date but it achieved no recognition or rewards.

Meanwhile, a mechanized adaptation of the original single punch tablet compressor made its appearance. A pulley on a drive shaft actuated an eccentric wheel which converted the horizontal rotary motion into a reciprocating vertical motion. In this way a plunger was pushed down repeatedly into a lower mold to which the powder was fed by an operator. This vertical machine was patented by Young in 1874. It did not have the speed of Bower's rotary press with its subsequent improvements.

Several other inventors, including Joseph Remington and Bennett L. Smedley, introduced small, manually operated, lever compression tablet machines, suitable for turning out relatively small quantities of tablets, but none of these compared in speed with the belt-driven rotary presses which were then being used by Wyeth in Philadelphia and in the plant of Davis and Lawrence in Montreal. Wyeth started manufacturing in the Davis and Lawrence plant in 1883 under an exclusive Canadian factor agreement which made Wyeth the first American manufacturer to establish a production unit in the Dominion.

Undoubtedly many unpatented improvements were quietly made in the tablet-making machinery that Wyeth used, but it took a fire which burned down the entire Wyeth plant in Philadelphia, on February 10, 1889, to provide the occasion for a break in the iron curtain of secrecy which had previously surrounded all Wyeth manufacturing activities.

"Death in the Flames" was the scarehead in the *Philadelphia Inquirer* followed by "Disastrous Fire in the Heart of the Fashionable Quarter" and "Wyeth Laboratory Destroyed." The scene was part of the present location of the Bellevue-Stratford Hotel.

Following the explosion of a quantity of chemicals in the rear of the manufacturing buildings, the firemen who had been fighting the blaze were forced to drop their hose and run for their lives under a rain of falling bricks. At a moment of utter demoralization, Director Stokley strode into the burning building and took immediate charge of the evacuation of all firemen. Two men had been pinned beneath fallen timbers, one of whom was rescued. The body of the other could not be extricated until several hours later.

That evening, a reporter from the *Philadelphia Press* called to interview John Wyeth who stated in response to questions that the loss would be about a half million dollars. The fire began in the basement of the retail drug store, originally Wyeth's own, which had been sold several years before to Frank E. Morgan so that the Wyeths could devote their entire attention to manufacturing and wholesaling.

"The precious formulas were saved," Wyeth vouchsafed. "The heaviest separate loss is on the pill presses. The pill pressing process is our own; we control it entirely."

Maxwell Wyeth, son of the senior member, was foreman of the pill presses. He said that he ran about 25 machines and that each machine could make about 120 pellets a minute (or 7,200 an hour). In the making of the pills about 60 men and girls were employed."

Wyeth, at its present day Philadelphia tablet department, has high speed tablet presses with a capacity varying now in use which varies from 21,000 to 60,000 per hour. On this basis the production of 1889 machines seems highly creditable.

Many other drug firms and machinery companies no doubt played an important part in the subsequent refinements of tablet-making and could contribute interesting facets about these developments from their own history. ■

innovations in percolation

by Gilman N. Cyr

THE process of percolation as applied to the extraction of drugs had its origins in Europe, but its full development as a procedure for the manufacture of extracts, fluidextracts and tinctures is largely attributable to American pharmacy. Outstanding pharmacists such as Procter, Diehl, Oldberg and Lloyd conducted experiments in extraction and made noteworthy contributions to the early development of percolation. Fluidextracts can be justly called American preparations because their development was due largely to American pharmacists.

Dr. Edward Robinson Squibb was prominent among the 19th century pharmacists who developed the process of percolation. In the very first paper which he was invited to read before the AMERICAN PHARMACEUTICAL ASSOCIATION in September, 1858, he suggested minor changes in five fluidextracts official in the *U.S. Pharmacopeia*.[1]

A native of Van Buren, Maine, Gilman N. Cyr earned his bachelor and master degrees at the Massachusetts College of Pharmacy. As a fellow of the American Foundation for Pharmaceutical Education at Purdue University, he gained his PhD degree in 1948. He returned to Massachusetts College of Pharmacy as assistant professor of pharmacy. Four years later, he joined Squibb, serving as research supervisor in the pharmaceutical research section of the Squibb Institute for Medical Research. Registered in Maine and Massachusetts, Cyr holds membership in Rho Chi, Sigma Xi, APhA, Society of Cosmetic Chemists and AAAS.

In his first paper on percolation[2] Dr. Squibb proposed a number of simple rules concerning the process but actually devoted the paper mainly to the presentation of two new pieces of equipment. One was a small automatic percolator with a reservoir of menstruum connected through a siphon to the top of the percolator (*Figure 1*). With enough menstruum in the reservoir a slow percolation could run for eight or nine days untouched. The other "simple contrivance" was the forerunner of the welltube or Squibb percolator. The particular advantage of this apparatus was that it replaced the easily broken percolator by a flat bottom vessel. In combination with the reservoir principle of the automatic percolator it became a manageable and convenient arrangement for large scale percolation.

During the Civil War period the country experienced a serious increase in the price of alcohol which threatened to interfere with the broad use of extracts and fluidextracts because of the greatly increased cost of preparing them.

The general plan of the *Pharmacopeia* for extraction was to exhaust the drug completely by percolation with an alcoholic menstruum and then to drive off the menstruum in whole or in part by evaporation. Dr. Squibb proposed instead[3] to exhaust the drug incompletely to the point at which the menstruum was of more value than the resulting extract obtained. In this manner he was sacrificing the cheaper drug rather than the dearer alcohol.

He first applied this plan experimentally to the extraction of colchicum seed, showing conclusively that a fluidextract equal to that of the *Pharmacopeia* could be made at a substantial saving. Similar successful experiments were carried out with other drugs representing seeds, roots and bark.

In 1866, as a member of the committee on the *Pharmacopeia*, Dr. Squibb presented to APhA some criticisms on the process for preparing fluidextract of buchu.[4] To economize on alcohol—but more to avoid heating the large amount of percolate used to exhaust the drug—he submitted a proposal which was the forerunner of fractional percolation. The drug was divided into three equal parts. The first portion was moistened with part of the alcoholic menstruum.

In July, August, and September of 1867 under the title "The Pharmacy of the Cinchonas" Dr. Squibb published a series of three papers in the *American Journal of Pharmacy*. In the first paper[5] of the series he criticized the menstruum, the preservative, and the potency of the official fluidextract. In the second paper,[6] he described a series of some 40 percolations designed to determine the optimum menstruum for the percolation of cinchona. When compared with diluted alcohol, the official 85 per cent alcohol not only extracted more total solids and more total alkaloids but also was much easier to handle and required much less heat to evaporate.

The final paper[7] was devoted to a presentation of formulas for many preparations of cinchona including the plain extract, the compound extract, the fluidextract, the compound fluidextract and others.

In August Dr. Squibb presented a paper on repercolation[8] before APhA. He stressed the importance of a fine powder and of using a larger quantity of alcohol to wet it before percolation. He also recommended that the first portion of percolate draining down be returned to the funnel for repercolation.

In previous discussions on percolation Dr. Squibb had often insisted that each drug was a case in itself and had to be studied to determine the best method and menstruum for its extraction. Consistent with this advice, he went next to a series of experiments on resin of podophyllum.[9]

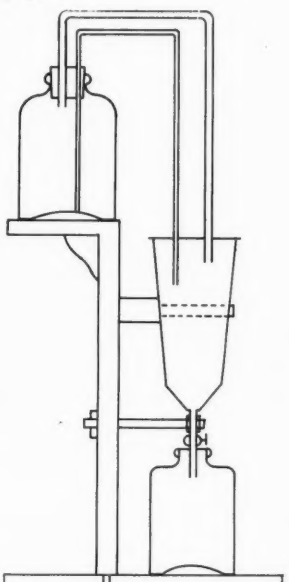

Figure 1—Small automatic percolator showing reservoir and siphon arrangement.

At the 1869 meeting of APhA Dr. Squibb, in commenting on the *U.S.P.*,[10] seriously questioned the advisability of continuing with a general process for percolation as applicable to all drugs suggesting instead a general commentary concerning the basic principles and equipment. He also criticized the directions given as usually ambiguous, inadequate and delusive in regard to practical exhaustion of the drug Adoption of the process of repercolation was recommended for the new revision of the *Pharmacopeia*. He suggested that the menstrua then used in various extractions were too weak in alcohol and in many instances better products would result with stronger alcohol and less of it.

At the following meeting, in 1870, he reported his studies on the extraction of nine important drugs.[11] These studies led him to the conclusion that the rate of exhaustion of a strange drug could not be predicted. They further emphasized a point made earlier that extraction was not uniform and the soluble components of a drug were not exhausted at the same rate. He stated rather unequivocally that to achieve complete extraction without the use of heat and with the least quantity of alcohol, repercolation was the only sensible process but admitted the difficulty of the process and the want of skill for its management.

Having had generally unsatisfactory results with the official process for fluidextract of senega, Dr. Squibb reported a thorough study of it.[12] The difficulties were associated with a rapid precipitation of polygalic acid and gelatinization of the fluidextract in cold weather. He found both of these problems to be functions of the menstruum. By including a small portion of ammonia, he was able to maintain the polygalic acid in solution and by increasing the concentration of alcohol, he was able to exclude much of the pectin which had been responsible for the gelatinization.

In 1872, Dr. Squibb exhibited a newly designed percolator which was intended to maintain some of the advantages of maceration in what was still essentially a percolation process.[13] With the new apparatus (*Figure 2*) he intended to create conditions more favorable to the passage of menstruum *through* the particles of drug rather than around them. The introduction of the apparatus was accompanied by a careful and detailed exposition of the theory on which it was based.

The whole arrangement was likened to a well dug in a wet soil of a substance to be percolated. The proposition was to pump out this well at so slow a rate that the liquid from outside the well coming in to supply this rate would descend so very slowly as to be frictionless. The object was to eliminate gravity flow to the extent that menstruum inside the particles of drug would descend as rapidly as menstruum outside these particles thereby maintaining uniform tension.

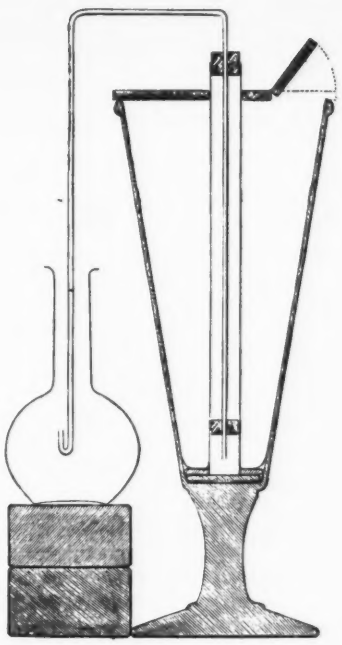

Figure 2—Small well-tube percolator with siphon in position for very rapid flow. In actual use siphon tube lifted much higher inside well-tube.

By this principle, Dr. Squibb was able to effect a greater economy in the use of alcohol and a better control on the rate of percolation. As with his previous designs, the controlling and unique element was a siphon which, in this instance, was used to control the rate of descent of percolate by controlling its removal from the well-tube. Although modified later in size, percolators based on this well-tube principle are still in use in the manufacturing laboratories of E. R. Squibb and Sons.

For six years, Dr. Squibb published nothing on percolation. Then, in 1878, at the request of the APhA committee on revision of the *Pharmacopeia* he presented a very lengthy report in which he reviewed much of his earlier work.[14] Because the report was intended to supply information for revision of the *Pharmacopeia* it was more detailed than any of his previous papers on this subject.

It had been shown many times that many of the official fluidextracts were not of the quality expected even when the official process was managed with great skill. Dr. Squibb had often demonstrated that repercolation could remedy this and he was concerned because it had not been applied by more people. He could only conclude that the process was considered too complicated by most pharmacists. His attempts to simplify the process without sacrificing the basic principles involved were not very successful. In the main, he could not eliminate the fractional collection of percolates, the need for multiple percolations and the necessity for reserving weak percolates for the following series.

Although repetitious in many respects, this paper made a unique and, by today's standards, an unparalleled contribution. It opened his formulary for all to see, giving very specific and detailed information for no less than 69 fluidextracts exactly as made in his laboratory.

This finally brought about official recognition of repercolation in the sixth revision of the *U.S.P.* in 1882. Having finally achieved this adoption, Dr. Squibb turned his attention to other matters and did not publish any more on percolation for the next 22 years.

Then in 1899 and 1900, the closing years of his life, he published four papers on the use of acetic acid as a menstruum for fluid extracts. Nux vomica,[15] cinchona,[16] belladonna root[17] and buckthorn and cascara[18] were chosen for study.

The last experiments with acetic acid were started just before Dr. Squibb's 80th birthday. An irregular heart and the lack of one hand did not put a stop to his experimentation. He still went to his laboratory with great regularity.[19] It appears likely that he planned to continue these studies to include all of the important drugs of the day, but on October 5, 1900, at the age of 81, Dr. Squibb passed away.

Such is the record of Dr. Squibb's contributions to this important phase of American pharmacy. Over a span of more than 40 years he worked to improve the process of percolation, bringing about changes in materials, in procedure and in equipment. Fluidextracts have been replaced by more highly refined isolates or by synthetic medicinals and percolation as an important pharmaceutical process has likewise receded. But percolation will always occupy an important position in the historical development of American pharmacy.

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some unique dosage forms

by Philo L. Burrin

As head of Eli Lilly and Company's pharmaceutical control department, Philo L. Burrin is responsible for four departments—the pharmaceutical inspection control department, formula control, printed materials control and finishing control. He has held this post since July, 1957. A native of Holgate, Ohio, Burrin joined Lilly as a pharmaceutical chemist on October 17, 1917, following his graduation from Purdue University. In his career with Lilly he has also been a bulk inspector, department head of biological vaccines and head of the pharmaceutical design department. He has contributed to the development of formula modifications, manufacturing technics and designing of equipment for new methods of testing. He is a past president of the Indianapolis branch of the American Pharmaceutical Association.

Glycones

GLYCERIN suppositories have been used for many years and have always presented a problem to the dispensing pharmacist because of their hygroscopic nature. The present *U.S.P. XV* includes a formula for their preparation consisting of 91 grams of glycerin, nine grams sodium stearate and five grams of purified water. The sodium stearate is dissolved in the hot glycerin, the water added and the mixture made ready for molding. This formula produces approximately 100 grams of finished product.

The mixture may be molded in various shapes and tightly closed glass containers. The effectiveness of these suppositories is, of course, dependent upon their glycerin content. However, an earlier formula which contained 95 per cent glycerin[1] resulted in the finished product's accumulating moisture on the surface more easily. To overcome this, our firm developed a means of preserving this product by dipping the finished suppositories into high-melting point parrafin wax. These "Glycones," as the suppositories were called, were marketed in 1890. They were quite stable and the paraffin coating was easily removed by scoring the middle of the Glycone with the thumbnail and slipping off each end of the case.

Rhubarb Fingers

Rhubarb root is a very old drug. The early supplies came from Asia, principally from China because the Chinese roots were better trimmed and appeared smoother. This drug was used considerably as an aperient in which a small portion of the root was administered orally and chewed. As a home remedy, it had the added advantage of being easily carried in the pocket of the patient. The smoothest, lightest-colored roots which were free from wormholes and other defects brought the highest market price and individual pieces of root were sold over the counter as such. To offer a uniform product of similar use, one which eliminated the necessity of the patient's selecting nice-appearing roots, we worked out a formula for preparing a product called "Rhubarb Fingers." This was prepared by grinding up high-grade rhubarb roots to a suitable powder and granulating it with dextrine, alcohol and water for compression on a conventional tablet machine into pieces approximately one-fourth inch by one-half inch by two inches, weighing approximately 82 grains. This allowed the druggist to supply a more uniform product for over-the-counter sale of rhubarb. Rhubarb Fingers were self-administered with the individual chewing a small portion of the compressed piece.

Alcresta Tablet of Ipecac

Ipecac has been used for more than four centuries as an emetic. This use too was probably established empirically. In later years the activity was isolated and emetine was considered to be one of the more active constituents. Subsequently, emetine was shown to be one of the few effective treatments for amebic dysentery, but its administration in therapeutic doses was most difficult because of its emetic properties.

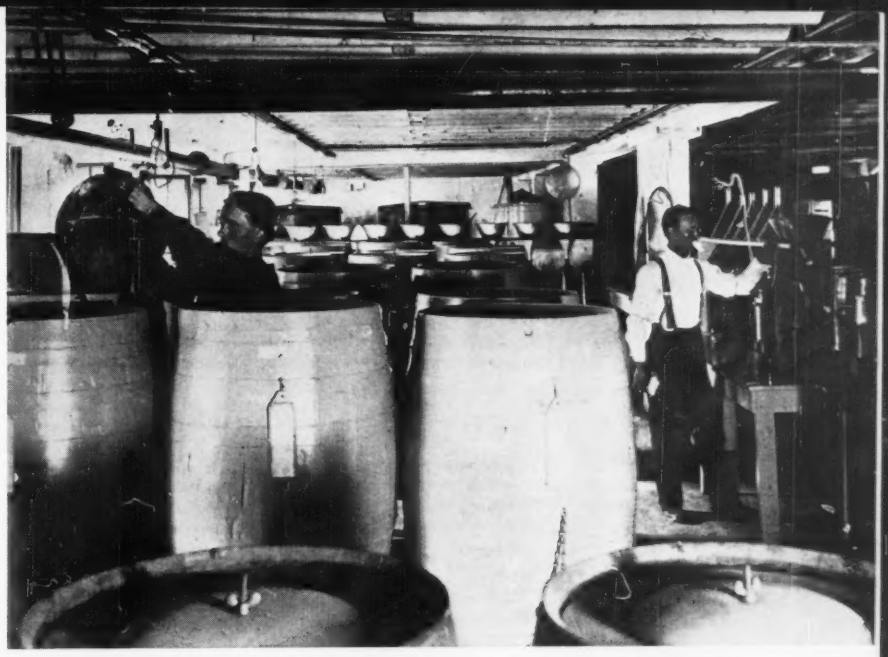
Our laboratories found the alkaloids of Ipecac could be adsorbed in Lloyd's Reagent, a natural-occurring hydrated aluminum silicate, named in honor of John Uri Lloyd, who discovered its qualities in 1910 and investigated its ability to adsorb alkaloids from acid solution. A patent was granted in 1912. With the alkaloids of Ipecac adsorbed on Lloyd's Reagent, it was possible to administer effective oral doses of these alkaloids since the acid secretion of the stomach prevented their release. The activity was released from the compound in the alkaline secretions of the intestinal tract. This served as an effective means of treating amebic dysentery by utilizing advantageously the enteric properties of the compound. Compressed tablets of this product, equivalent to ten grains of Ipecac U.S.P., were marketed under the name "Alcresta Tablets of Ipecac."

Liquid Blaud

In a communication to the *Bulletin General de Therapeutique of Paris* (September, 1831), a Dr. Cottereau stated that a provincial medical man had reported earlier to the Academie Royale de Medecine the composition of certain pills which he had found efficacious in cases of chlorosis.[2] Early in 1832, there appeared in the same journal a protest from Dr. Blaud, head physician of the Hospital of Beaucaire, Gard, and a corresponding member of the Academie Royale de Medecine, explaining that the formula published by Dr. Cottereau was not identical to the one he had devised. An authentic formula given by Dr. Blaud was one gram of sulfate of iron and one gram of potassium carbonate in a fine powder. This mixture was made into pills using tragacanth and powdered licorice. Later on, this was modified by adding honey to the pill mass to prevent rapid oxidation of the mixture. Blaud pills enjoyed great popularity and their effectivensss due primarily to the freshness of the ferrous carbonate, indicated that the partially oxidized product was not quite as effective in the treatment of certain anemias.

In 1907 our company marketed a product known as "Liquid Blaud"

which was designed to take advantage of the administration of freshly precipitated ferrous carbonate. In this product the ingredients, ferrous sulfate and potassium carbonate, were dissolved in glycerin, a clear solution that could be maintained over a long period of time. When a dose of one teaspoonful (96 min.) was added to water (one to four fluid ounces), the ferrous carbonate was immediately precipitated as a green flocculent precipitate. This mixture was administered orally; and, because of the freshness of the precipitated ferrous carbonate, it was highly beneficial in certain types of anemias. Furthermore, it was possible to dissolve two other medicinal agents, useful in the treatment of anemia, namely arsenic and strychnine, in this glycerin solution and thereby add to the therapeutic dose. The stability of the glycerin solution further could be enhanced by overlaying the solution with a thin layer of mineral oil. When the drug was dispensed, the bottle was thoroughly shaken before the dose was poured out. This dose contained only a proportionate part of the mineral oil so that when the bottle was stoppered and returned to rest, the remaining mineral oil came to the top and served as a protective coating to prevent oxidation by air.



An actual photograph of the Eli Lilly and Company plant about the turn of the century.

All of these products have been deleted from the current price list. In most cases they have been supplanted by more specific and perhaps more highly scientific pharmaceutical products. ■

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American Association for Advancement of Science

126th Meeting—Chicago, Illinois, December 26–30, 1959

Program of the Section on Pharmacy

SATURDAY, DECEMBER 26

8:00 p.m.—AAAS General Symposium Moving Frontiers of Science IV: Part 1.

SUNDAY, DECEMBER 27

2:00 p.m.—AAAS General Symposium Moving Frontiers of Science IV: Part 2.

MONDAY, DECEMBER 28

9:00 a.m.—*George L. Webster*, Dean, College of Pharmacy, University of Illinois, presiding.

1. Assembly and Operating Characteristics of Improved 4 Pi Liquid Scintillation Counter—*Billy G. Dunavant, John E. Christian*, Purdue University, Bionucleonics Department.
2. Quenching of Fluorescence in Liquid Scintillation Counting of Labeled Organic Compounds—*C.T. Peng*, University of California Medical Center. Radioactivity Research Center and School of Pharmacy.
3. Application of Neutron Activation Analyses to Micro-Analyses of Gold-Containing Pharmaceuticals in Biological Materials—*James P. Vacik* and *John E. Christian*, Purdue University, Bionucleonics Department.
4. Tetrahydroquinolizinium Salts I, Method of Synthesis of 2-Hydroxy-3-Bromoquinolizinium Bromide—*K.M. Wischmann*, Thiokol Chemicals; *A.V. Logan*, Oregon State College, Department of Chemistry; *D.M. Stuart*, Oregon State College, School of Pharmacy.
5. Color-Coding of Solid Drug Dosage Forms by Means of C.I.E. Trichromatic Coefficients—*Robert G. Brown*, University of Texas, College of Pharmacy.
6. Hydration of Procaine Base—*W.A. Strickland, Jr.*, University of Arkansas, School of Pharmacy.
7. Method for Evaluating Availability of Aspirin from Enteric Coated Tablets—*Joseph V. Swintosky, Rudolph H. Blythe*, Smith Kline and French Laboratories.
8. Physical-Chemical Basis of Buffered Aspirin Controversy—*Gerhard Levy, Barbara A. Hayes*, University of Buffalo, School of Pharmacy.
9. Evaluation of Suppository Bases—*Joachim Anschel*, Warner-Lambert Research Institute.
10. Solubilization of Riboflavin by Complex-Formation with Caffeine, Throphylline, and Dimethyluracil—*David E. Guttman*, Ohio State University, College of Pharmacy; *Manohar Y. Athalye*, Bombay, India.
11. Interactions of Xanthine Molecules with Serum Albumin I; binding of Caffeine by Bovine Serum Albumin—*M.L. Eichmann, D.E. Guttman, E.P. Guth*, Ohio State University, College of Pharmacy.
12. Binding of Drugs by Plastics III; Effect of pH and Solvents on Interaction of Sorbic Acid with Nylon—*Z.I. Shaikh, A.J. Kapadia, J. Autian*, University of Michigan, College of Pharmacy.
13. Isolation and Characterization of New Amino Acid: B-Amino-α-Phenylpropionic Acid—*Egil Ramstad, Allan M. Goodeve*, Purdue University, School of Pharmacy.
14. Origin of Tropic Acid Moiety of Hyoscyamine—*Allan M. Goodeve, Egil Ramstad.*
15. Research on Psychopharmacologic Drugs—*John O. Meany*, Santa Monica, California.

MONDAY, DECEMBER 28 (*Continued*)——**Scientific frontiers highlight opening session**

2:00 p.m.—*John Autian*, Professor, College of Pharmacy, University of Michigan, presiding.

1. Social Psychology of Prescription Writing—*Esther J.W. Hall*, University of Texas, College of Pharmacy; *Norman G. Hawkins*, Medical Branch Department of Preventive Medicine, Galveston.
2. Phenylalanine, Precursor of Berberine—*Jack L. Beal*, Ohio State University, College of Pharmacy; *Egil Ramstad*.
3. Incorporation of Mevalonic Acid Into Digitoxigenin—*Egil Ramstad, Jack L. Beal*.
4. Application of Paper Chromatography and Electrophoresis to Assay of Pharmaceutical Products—*Herbert Schriftman, Robert C. Shultz*, Wyeth Laboratories.
5. Study of Fate of Tumor Implant on Rats Using Cells Labeled with Sulfanilic-S^{35} Acid—*C.T. Peng*.
6. Comparative Study of Analgesimetric Methods—*Albert I. Edlin, Arthur Tye, John W. Nelson*, Ohio State University, College of Pharmacy.
7. Effects of Physostigmine on Egg Day Survival of Chloramphenicol Treated Embryonated Chick Eggs—*Vernon A. Green*, University of Texas, College of Pharmacy.
8. Distribution of C-14 Meprobamate in Rat Brain—*John L. Emmerson, Tom S. Miya, George K.W. Yim*, Purdue University, Department of Pharmacology.
9. Pharmacological Prevention of Acute Heart Failure from Neuromuscular Stress in Rats Conditioned for Cardiac Necroses—*John W. Ingalls, Jr., Samuel L. Friedman*, Long Island University.
10. Metabolism of Glycolic Acid-1-C^{14} in Rat Liver—*F.D. O'Connell, Egil Ramstad*, Purdue University, School of Pharmacy.
11. Presence of β-Glucoside (Lonicerin) in Honeysuckle and its Spontaneous Conversion to an Acid—*M.R. Shastri, Egil Ramstad*, Purdue University, School of Pharmacy.
12. Effect of Freeze-Drying on Constituents of Podophyllum Root—*Mahenc Shah, Earl P. Guth*, Ohio State University, College of Pharmacy.
13. Urease and Citrase Production by Pathogenic Gram Negative Bacilli—*H. Seneca, C.K. Troc, P. Milner*, Columbia University, Department of Urology, College of Physicians and Surgeons.
14. Law of Initial Value in Pharmacology—*Joseph Wilder*, New York Medical College, Neurology Department.
15. Theory of Relativity and Arterial Failure—*Harry Lobel*, Omaha, Nebraska.
16. Biological Effects of Magnetic Fields (I, General)—*M.F. Barnothy, J.M. Barnothy*, University of Illinois, College of Pharmacy.
17. Biological Effects of Magnetic Fields (II); Treatment of Cancers and Radiation Syndrom—*J.M. Barnothy* and *M.F. Barnothy*, University of Illinois, College of Pharmacy.

TUESDAY, DECEMBER 29——**Hospital pharmacy takes over discussion.**

9:00 a.m.—Hospital Pharmacy; *Joseph Oddis*, presiding.

Opening Remarks and Announcements—*John E. Christian, Secretary*, Section Np.

1. Greetings—American Society of Hospital Pharmacists, American Pharmaceutical Association, Illinois Society of Hospital Pharmacists, College of Pharmacy, University of Illinois, American Hospital Association.
2. Application of Closed System Technics in Environments Related to Hospital Services—*Kenneth R. Nelson, Jr.*, Division of Special Health Services, U.S. Public Health Service.
3. Solubilization of Iodine with Tween 20—*Edward N. Deeb*, Veterans Administration Hospital, Pittsburgh.
4. Administrative Determinations and Policies Relative to Use of Radioactive Medications and Investigational Drugs in Hospitals—*Milton W. Skolaut*, Pharmacy Department, *Dr. Robert M. Farrier*, Clinical Center, National Institutes of Health.
5. Hospital Association—Hospital Pharmacist Liaison—*David M. Kinzer*, Illinois Hospital Association.
6. Solvency of Hospitals—A National Economic Problem—*George M. Scattergood*, Armstrong Cork Company.
7. Some Social Forces That Will Affect Hospital and Hospital Pharmacy—*Ray E. Brown*, University of Chicago Clinics.
8. Joint Committee of AHA and ASHP and Its Role in American Hospital Pharmacy—*George F. Archambault*, Pharmacy Branch, Division of Hospitals, U.S. Public Health Service.

12:20 p.m.—Tour American Hospital Association, Headquarters Building.

2:00 p.m.—Address of *Vice President* and *Chairman, Glenn L. Jenkins*, Dean, School of Pharmacy, Purdue University. Hospital Pharmacy; *George F. Archambault, presiding*.

1. Patient Oriented Hospital Standards—Realistic Approach to State Regulation—*Oliver J. Neibel, Jr., Phillip A. Austin*, Washington State Department of Health; *Al Bailey*, Washington Board of Pharmacy, Seattle.
2. Pharmacist's Role as Drug Consultant in Hospital—*Donald C. Brodie*, San Francisco Medical Center.
3. Pharmacist's Role in Nursing Education—*Eleanor C. Lambertsen*, Council on Professional Practice, AHA.
4. Hospital Pharmacy Planning—*Paul F. Parker*, Division of Hospital Pharmacy, APhA.
5. Drug Name Integrity—*Wm. E. Woods*, National Pharmaceutical Council, Inc.
6. Principle of Prior Consent in Formulary System—*Don E. Francke*, Michigan University Hospital.
7. Role of French Military Pharmacist as Debated in Academy of Medicine in Paris during 1873—*Alex Berman*, University of Michigan.
8. Statistical Findings and Interesting Case Reports—*Henry L. Verhulst*, National Clearinghouse for Poison Control Centers, U.S. Public Health Service.

WEDNESDAY, DECEMBER 30——**"Scientists' Part in Protection of Public" themes symposium.**

1:30 p.m.—Symposium: Scientist's Part in Protection of the Public, Part I (Food, Drug, Cosmetic and Hazardous Chemical Problems); *Joseph V. Swintosky*, Smith, Kline and French Laboratories, presiding.

1. Labeling of Hazardous Chemicals—Help or Hindrance—*Bernard E. Conley*, Secretary, Committee on Toxicology, American Medical Association.
2. Pharmaceutical Ingredients Legislation, Problems and Approaches to Solving Them—*William F. Bousquet*, Assistant Professor of Bionucleonics, Purdue University.
3. Role of Cosmetic Scientist in Protecting Public Health—*Raymond E. Reed*, Vice President, Toni Company.
4. Applications of Radioisotope Tracer Technics to Studying Food Additive Problem—*John H. Rust*, Professor of Pharmacology, Head, Section of Nuclear Medicine, University of Chicago.
5. Problems in Evaluating Safety of Intentional Food Additives—*O. Garth Fitzhugh*, Chief, Toxicity Branch, Division of Pharmacology, Bureau of Biological and Physical Sciences, Food and Food Administration.

8:00 p.m.—Symposium: Scientist's Part in Protecting Public, Part II (Food Additive Legislation); *Glenn L. Jenkins*, presiding.

1. Problems in Evaluating Safety of Unintentional Food Additives—*A.J. Lehman*, Director, Division of Pharmacology, Bureau of Biological and Physical Sciences, Food and Drug Administration.
2. Scientific Judgment in Law and Regulation—*Edward J. Matson*, Director of Scientific Administration, Abbott Laboratories.
3. Role of Scientific Expert Under Present Food Laws—*Bernard L. Oser*, President, Food and Drug Research Laboratories, Inc.
4. Question Session.

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antibiotics symposium

THE CHALLENGE of New Drugs in Our Society" was the basic theme of the opening session of the seventh annual Symposium on Antibiotics held November 4–6, 1959 in Washington, D.C. The three-day program considered 246 reports on recent investigations and developments in antibiotics and several other drugs, with scientists from 22 countries beside the U.S. being represented among the participants.

The enormous number of new drugs being made available reflects the energy and effort directed by the pharmaceutical industry to research and development. This challenge of new drugs, stated Chairman Henry Welch, is perhaps the most difficult challenge medicine has ever encountered.

The modification of medical habits resulting from the developments in chemotherapy was discussed by Dr. Austin Smith. Dr. Smith noted that the results of the new developments for the benefit of the sick are evident but their significance is not generally understood; and this causes confusion which confounds the problems of the public, the legislators, the press, and even the health professions and the makers of drugs. He observed that many of the problems faced by the drug manufacturers today are, ironically, due to the very successful efforts of those same groups in developing drugs which prevent and cure illness as well as allaying the inactivating symptoms of aging.

Yearly reviews of basic drugs were recommended by Dr. J.J. Curry, who spoke on the practicing physician's appreciation and application of newer drugs and therapy. He observed that the reviews should be published by the AMA Council on Drugs because it is not sufficient to determine only that a drug is safe and has some effectiveness.

This theme was further developed by Dr. Maxwell Finland. He deplored the many reports on new drug effectiveness that are not based upon properly planned and designed clinical trials. He stressed the need for an objective approach to the selection of patients, proper blind technics of drug application and scientific methods of evaluating the results of therapy. Dr. Finland recommended less haste in marketing new drugs before adequate clinical testing has been completed and evaluated.

Some of the new antibiotics reported at the symposium are colistin, aspartocin, fervenulin, streptozotocin, and rifomycin. Colistin, discovered by Koyama, *et al.*, in Japan, has been used as colistin sulfate and sodium colistin methanesulfonate for several years in Japan, Italy, and France, and for the past year clinically in the U.S. Rifomycin, isolated and studied by Lepetit S.p.A. (Italy) researchers, has been separated into its stable and highly acid component rifomycin B and the remaining rifomycin-complex (most active components rifomycin C and D). Rifomycin B forms soluble neutral salts with inorganic and organic bases as well as esters and ethers. It is reported to have low activity but also very low toxicity and therefore a favorable therapeutic index.

Reports on antitumor agents included the new antibiotics diazomycin (A, B, and C) and streptonigrin. Some hopeful clinical results have been obtained with the latter. Further studies in this field with actinobolin, streptovitacin, the nonantibiotic agent cyclophosphamide, and extensive Japanese clinical trials with mitomycin C were presented.

New tetracycline derivatives included demethylchlortetracycline (permits lower dosage) and pyrrolidinomethyl tetracycline which appears to lend itself to the formulation of parenterals that cause less pain and tissue damage at the injection site. New uses were described for paromomycin, amphotericin and griseofulvin.

An outstanding development reported at the symposium by Bristol researchers was the synthesis of potassium (alpha-phenoxyethyl) penicillin by acylation of 6-aminopenicillanic acid with alpha-phenoxypropionic acid. Chairman Welch observed that the new penicillin (one of many synthesized) is better absorbed by man than either penicillin G or penicillin V; differing from the latter (phenoxymethyl penicillin) by one additional methyl (CH_3) group. From the chemotherapeutic viewpoint, Dr. Welch noted that the addition of a CH_3 group to penicillin V increased its ability to be absorbed by man; while, in another laboratory (Lederle) the removal of a CH_3 group from chlortetracycline (to obtain demethylchlortetracycline) accomplished a similar improvement in absorbability. He doubted that these two developments represented an "industry trading" of CH_3 groups.

The successful synthesis of many penicillins suggested that the key may be found "to open the door to a broad spectrum penicillin, to antifungal penicillins, antiviral penicillins, or even to penicillins active against tumor cells by the correct manipulation of the guiding side chain."

Obituaries

Dr. Walter Hollis Eddy, pioneer in vitamin and nutrition research, 82, died in Lake Worth, Florida, on September 28. He was professor emeritus of physiological chemistry at Teachers College at Columbia Univeristy, an author on vitamin research and a consulting chemist. For the last ten years he had been research consultant to the U.S. Vitamin and Pharmaceutical Corporation, New York City.

In 1924, Dr. Eddy isolated pure crystalline biosy vitamins found in, and necessary for, the growth of yeast. Recently, with Dr. Boris Sokeloff of Southern Biological Research Laboratory, he reported that a water-soluble, citrus fruit bioflavonoid compound had proved effective in arresting bleeding from capillaries, and was observed to slow growth of cancerous tissue.

Dr. Charles R. Jacobsen, 31, director of chemical research for the Knoll Pharmaceutical Company of Orange, New Jersey, passed away on Monday, November 9, following a brief illness. A member of APhA and the American Chemical Society, Dr. Jacobson was also active in church and civic affairs in his home community of Scotch Plains, New Jersey. After completing his graduate study at Lehigh University, he devoted himself to research in the field of medicial chemicals. He is survived by his wife, two sons, his parents and a sister.

COOPERATION

on the German and/or European Market

Which manufacturer of a pharmaceutical preparation successfully introduced in the USA is interested in producing it in Germany?

We are setting up a new factory in Southern Germany and could still consider your special requirements. We have already an efficient sales organization, with salesmen calling on pharmacies and drugstores.

Therefore, you need not invest any capital in manufacturing premises nor in distribution.

Exchange for a preparation well introduced in Germany would also be considered.

Please write by airmail to **box Z. K. 8659 c/o Annoncen-Expediton Hans Kegeler, Berlin-Wilmersdorf, Nikolsburger Strasse 10, Germany.**

Calendar of Events

DECEMBER

7–9 Pharmaceutical Manufacturers' Assn., eastern regional midyear meeting, Waldorf-Astoria Hotel, New York, N.Y.
9 Remington Medal Dinner honoring Justin Powers, Roosevelt Hotel, New York, N.Y.
9–11 Proprietary Assn. midwinter meeting, small volume forum, Biltmore Hotel, New York, N.Y.
10 National Pharmaceutical Council annual meeting, Pierre Hotel, New York, N.Y.
26–31 American Assn. for Advancement of Science annual meeting, Chicago, Ill.

1960

JANUARY

6 New York Cosmetic Chemists meeting, Hotel New Yorker, New York, N.Y.
7 National Drug Trade Conference, Washington, D.C.
13 Associated Chain Drug Stores Assn. meeting, Drake Hotel, Chicago, Ill.
18 National Assn. of Chain Drug Stores meeting of active members, Savoy-Hilton Hotel, New York, N.Y.
20 Massachusetts Pharmaceutical Assn. midwinter conference, Hotel Bancroft, Worcester, Mass.
21 District of Columbia Pharmaceutical Assn. general membership meeting, The Broadmoor, Washington, D.C.
23–24 Midwest Conference of Pharmaceutical Assns., Hotel President, Kansas City, Mo.
27 New Jersey Pharmaceutical Assn. annual midwinter meeting, New Irvington Hotel, Lakewood, N.J.

FEBRUARY

3–5 Pharmaceutical Manufacturers' Assn., legislative section, Boca Raton, Fla.
4 Michigan State Pharmaceutical Assn. midseason meeting, Whitcomb Hotel, St. Joseph, Mich.
8–10 Pharmaceutical Manufacturers' Assn., central regional meeting, Edgewater Beach Hotel, Chicago, Ill.
14–17 American College of Apothecaries annual convention, Hotel Americana, Bal Harbour, Fla.
15–16 Pharmaceutical Manufacturers' Assn., western regional meeting, Ambassador Hotel, Los Angeles, Calif.
25–26 Pharmaceutical Manufacturers' Assn. traffic conference dinner and workshop, Hotel Biltmore, New York, N.Y.

MARCH

2–4 Pharmaceutical Manufacturers' Assn., medical section, Hollywood Beach Hotel, Hollywood, Fla.
3 Drug, Chemical and Allied Trades Assn., New York Board of Trade, Inc., annual dinner, New York, N.Y.
3–4 Federal Wholesale Druggists' Assn. midyear get-together, Statler-Hilton Hotel, New York, N.Y.
6–8 Iowa Pharmaceutical Assn. annual convention, Roosevelt Hotel, Cedar Rapids, Iowa.
13–18 National Health Forum (National Health Council), Miami, Fla.
20–22 Kansas Pharmaceutical Assn. annual convention, Topeka, Kan.
26 National Conference State Pharmaceutical Assn. Secretaries, Statler-Hilton Hotel, Washington, D.C.
27–28 APhA House of Delegates, Statler-Hilton Hotel, Washington, D.C.
29–30 USP decennial meeting, Statler-Hilton Hotel, Washington, D.C.

APRIL

13–15 American Public Health Assn., southern branch, Memphis, Tenn.
17–20 Georgia Pharmaceutical Assn. convention, Hotel DeSoto, Savannah, Ga.
18–20 National Assn. of Chain Drug Stores biennial convention, Hollywood Beach-Diplomat-Seacrest Hotels, Hollywood, Fla.
23–25 Arizona Pharmaceutical Assn. annual convention, Stardust Hotel, Yuma, Ariz.
24–26 Nebraska Pharmaceutical Assn. annual convention, Hotel Yancey, Grand Island, Nebr.

MAY

8–10 North Carolina Pharmaceutical Assn. annual convention, Robert E. Lee Hotel, Winston-Salem, N.C.
15–18 Florida State Pharmaceutical Assn. annual convention, Hillsboro Hotel, Tampa, Fla.
15–18 Ohio Pharmaceutical Assn. annual convention, Biltmore Hotel, Dayton, Ohio
15–20 National Tuberculosis Assn., Statler and Biltmore Hotels, Los Angeles, Calif.

JUNE

6–8 Colorado Pharmacal Assn. annual convention, Antlers Hotel, Colorado Springs, Colo.
6–8 Michigan State Pharmaceutical Assn. annual convention, Statler-Hilton Hotel, Detroit, Mich.
9–12 American Therapeutic Society, Barcelona Hotel, Miami Beach, Fla.
11–12 American Diabetes Assn., Inc., Hotel Deauville, Miami Beach, Fla.
13–16 Tennessee Pharmaceutical Assn. convention, Gatlinburg, Tenn.
13–17 American Medical Assn. annual meeting, Miami Beach, Fla.
19–21 Massachusetts Pharmaceutical Assn. annual convention, New Ocean House, Swampscott, Mass.
19–22 Virginia Pharmaceutical Assn. annual convention, Virginia Beach, Va.
19–23 New Jersey Pharmaceutical Assn. annual convention, Hotel Traymore, Atlantic City, N.J.
21–23 Indiana Pharmaceutical Assn. annual convention, French Lick-Sheraton Hotel, French Lick, Ind.
22–24 District of Columbia Pharmaceutical Assn. annual convention, Commander Hotel, Ocean City, Md.
27–30 Maryland Pharmaceutical Assn. annual convention, Shelburne Hotel, Atlantic City, N.J.

JULY

25–27 Texas Pharmaceutical Assn. annual convention and exhibit, Municipal Auditorium, Austin, Tex.

AUGUST

14–19 American Pharmaceutical Assn. annual convention, Washington, D.C.
27–Sept.1 American Hospital Assn., Civic Auditorium, San Francisco, Calif.

SEPTEMBER

15–18 Drug, Chemical and Allied Trades Assn. annual meeting, Sagamore Hotel, Bolton Landing, N.Y.
18–21 Federal Wholesale Druggists' Assn. annual convention, Greenbrier Hotel, White Sulphur Springs, W.Va.

OCTOBER

14–20 National Wholesale Druggists Assn. meeting, American Hotel, Bal Harbour, Fla.
31–Nov.2 Packaging Institute annual forum, Statler-Hilton Hotel, New York, N.Y.

INTERNATIONAL

1960

MAY

2–11 Pan American Medical Assn. Congress, Mexico, D. F., Mexico (Section on Pharmacology and New Drugs, J.C. Munch, Secretary)

AUGUST

28–Sept.2 18th General Assembly of International Pharmaceutical Federation, Copenhagen, Denmark

NOVEMBER

13–19 5th Pan-American Congress of Pharmacy and Biochemistry, Santiago, Chile

Our Very Best Wishes
At
Christmas Time

THE AMERICAN DRUGGISTS'
INSURANCE COMPANY

Cincinnati 3, Ohio

Federal and State Actions

FDA Actions

Illegal Over-the-Counter Sales for the Month of October

Arizona—Herbert C. Brightbill, pharmacist, and Herman M. Hoffman, pharmacist, (employees of Consumers Market), Tuscon—Refilling prescriptions for barbiturates, cortisone and tranquilizers without doctor's authorization. Imposition of sentence deferred one year and each defendant placed on one-year probation.

Richard L. Gibson, t/a Eureka Drugs, and Morris Rosenthal, pharmacist, Tucson—Selling amphetamine, barbiturates, cortisone and tranquilizers without doctor's authorization. Imposition of Gibson sentence deferred six months; defendant placed on six-month probation. Imposition of Rosenthal sentence deferred one year; defendant placed on one-year probation.

T. Ed Litt Drug Company, Inc., a corporation, C. Aubrin Anderson, pharmacist, and Roy Petersen, pharmacist, Tucson—Refilling prescriptions for barbiturates, cortisone and thyroid tablets without doctor's authorization. Imposition of sentence deferred for one year and defendants placed on one-year probation.

Colorado—L.E. Hillman, D.O., Brush—Dispensing barbiturates not in the course of professional practice. Fined $300.

Adolphus Adams, t/a Adams Drug, and George J. Lohmiller, pharmacist, Pueblo—Selling and refilling prescriptions for antibiotics and tranquilizers without a doctor's authorization. Lohmiller fined $125, placed on one-year probation. Action against Adams not yet settled.

Massachusetts—Hemenway Drug Company, and Nicholas T. Elias, president and treasurer, and Charles Bowen, assistant manager, Boston—Refilling prescriptions for sedatives, sulfonamides and tranquilizers without doctor's authorization. Corporation fined $300; Elias $200; Bowen, $100.

Nebraska—Harry G. Williams, MD, Omaha—Selling amphetamine not in the course of professional practice. Fined $1,000 plus $38.20 costs; placed on three-year probation, with one-year suspended sentence.

New York—Friendly Drug Stores, Inc., and Max Allshut, president, Ridgewood—Selling and refilling prescriptions for amphetamine, hormones and tranquilizers without a doctor's authorization. Corporation fined $1,000; Allshut, $1,000.

Martin Harnick, t/a Martin Drugs, Ridgewood—Selling and refilling prescriptions for amphetamine, hormones and tranquilizers without doctor's authorization. Fined $1,000.

North Carolina—Allen Drug Company, and Harry H. Allen, Sr., and William Franklin Allen, partners, Cherryville—Selling antibiotics and barbiturates without doctor's authorization. Partnership fined $1,000, each defendant placed on three-year probation.

Texas—First Street Drug Store, Inc., and Fred E. Simmons, president, Irving—Selling amphetamine, antibiotics, barbiturates and cortisone without a doctor's prescription. Corporation fined $250; Simmons, $250.

Misbranded Drugs

Missouri—Lloyd C. Shanklin, t/a Harmony Health Foods and Juices, Kansas City—Aloe leaves and papaya were misbranded orally and by booklet, with false claim for the treatment of disease. Shanklin sentenced to two years' imprisonment.

Preliminary Injunction

New York—Wilson Williams Company, Inc., and Jack Elliott, president, Tuckahoe—From selling in interstate commerce RX-120 (a drug labeled with weight reduction claims alleged to be false and misleading).

Vitamin E Claims

FDA has cautioned consumers against wild claims about products purporting to be sources of vitamin E. Since the daily diet provides more than adequate amounts of vitamin E for the average individual, supplementing it with the vitamin is not necessary. Products represented as containing vitamin E are no longer required to bear a label statement that the need for this vitamin in human nutrition has not been established, since it has now been established that vitamin E is needed in the physiological processes of the human body.

FDA has warned against claims that products offered as sources of vitamin E are necessary to treat or prevent any identifiable nutritional deficiency. A number of court actions have been taken against vitamin E products promoted for treating or emphasizing such diseases as sterility, heart disease and muscular dystrophy. FDA said that the vitamin is of no value for such purposes. "Any claim in the labeling of drugs or of foods offered for special dietary use by reason of vitamin E, that there is need for dietary supplementation with vitamin E, will be considered false," the FDA said in its announcement of October 29, 1959.

Enurtone Device—Claims

The Federal Trade Commission, on October 16, 1959, ordered the Enurtone Co. to discontinue falsely advertising that its Enurtone device will stop all cases of bed-wetting. FTC Commissioner W.C. Kern said: "The public interest plainly requires that such claims or promises for helping enuritics as may be in respondents' future promotional matter be limited to cases of enuresis for which benefits reasonably may be expected to be afforded."

Misuse of Tes-Tape

FDA Commissioner George P. Larrick warned that test papers chemically treated with tolidine, which are properly and effectively used to detect urine sugar in diabetes, should not be used to detect the presence of sugar in the cervix as an indication of ovulation (fertility cycle) "until appropriate tests have been conducted to show that [internal] use of the paper will not cause injury. . ." FDA emphasized that Eli Lilly, the manufacturer of the paper (Tes-Tape), has not recommended its product for testing fertility. However, two other firms have marketed plastic devices for applying the papers to the cervix; and while these firms are no longer recommending use of the tolidine-treated papers, FDA is concerned lest women who already have a supply on hand may continue to use it. There is no question about the safety of the use of Tes-Tape in the urine sugar test.

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is seeking scientists as section heads for this aggressively expanding department. Key positions now open:

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Ph.D. preferred but not essential. Significant related practical experience.

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Ph.D. essential, preferaly in physical chemistry. Truly creative man with related experience in drug field.

Please send detailed resume in complete confidence. All replies will be acknowledged. Our employees know of this ad. **Box No. P 12-1.**

Letters

No Change in Policy

Sir:

I have just received volume 20, number 11 of the APhA JOURNAL and I'm a little upset. On page 641 there is a picture of some naval pharmacy trainees being entertained by a drug manufacturer. Please don't misunderstand me—I'm not upset at the manufacturer by any means. What bothers me more is the two-facedness of the JOURNAL. After many years of proposing that the Armed Forces should use registered pharmacists in equivalent positions in the Army and Navy, your magazine does an about face and shows 'trainees' being entertained. I assume that some of these 'trainees' might actually be registered pharmacists; I further assume that most are not.

This instance—however trivial—certainly does not help to further the cause of placing pharmacists in the Armed Services in positions for which they are certainly more qualified than a 'trainee.' I am sure that the Navy does all it can to train these men well. They will not be, however, registered pharmacists in the true sense of the word. I feel that further publication of instances like this will do great harm to the profession in general and to those men who are proud well-trained members of that profession.

Nathan W. Rodnon
Jersey City, N.J.

Editor's Note. The inclusion of the photograph of Naval Pharmacy Trainees on page 641 of our November issue does not represent a change in the ASSOCIATION'S policy against "trainee pharmacy programs." It is only our way of alerting our readers to the fact that we are not making the progress we should with regard to the status of pharmacists in the military service. Our many editorials on this subject have largely fallen on deaf ears, and we hope that the photograph on page 641 will be disturbing to many more of our members so that, in addition to writing us, they will voice their protests against the "trainee pharmacy programs" to the Defense Department.

Orchids to Articles

Sir:

I enjoyed reading the article "What does medical care cost?" and would like if possible ten reprints so that the general public could understand that the cost of medicine is inexpensive as compared with other expenditures. I am sure if the general public knew the facts about the bargain they were getting on drugs there would be no need to explain the price of every prescription. I would like to thank you for the reprints at this time and also on the article which is important to every pharmacist.

David J. Foy
Belleville, Ill.

Sir:

If reprints of the following articles are available, please advise me as to quantity and price:

1. What does medical care cost?
2. Science works for better community health
3. People demand good health facilities

The above articles were well presented, timely, and of vital interest to all of us connected with the professional teams serving in public health.

W.A. Scribner, Jr.
Pasadena, Calif.

Editor's Note. Single copies of these reprints are available from the American Pharmaceutical Association at no charge; quantity prices are $10 per hundred and $80 per thousand.

Sir:

I was delighted to be a part of what is an exciting example of good makeup and interesting journalism.

Austin Smith, M.D.
Washington, D.C.

Typical case studies convincingly portray the therapeutic action of

MAZON OINTMENT
and MAZON SOAP

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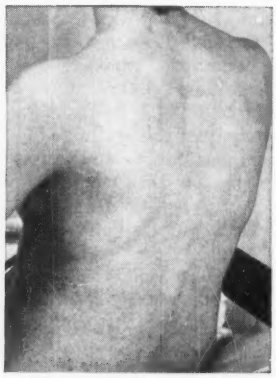

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ECZEMA
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and other skin disorders

MAZON — has the widest sphere of application in the treatment of skin diseases and is comfortingly free from side re-actions.

MAZON — Ointment and Mazon Soap have been highly successful in the treatment of obstinate skin conditions that fail to respond to other preparations.

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Physicians have proved to their own satisfaction the unusual effectiveness of Mazon. *We invite you to try the MAZON dual therapy.*

BELMONT LABORATORIES CO.
PHILADELPHIA, PENNA.

Prescription Practice *by Samuel W. Goldstein*

℞ *Information Service*

Aluminum Methionate

See THIS JOURNAL, **20,** *614(Oct., 1959) for a note on the preparation of Aluminum Methionate.*

A reader has called our attention to the fact that Aluminum Methionate is available commercially from the R.S.A. Corporation, Ardsley, New York. The compound was included in a formula for a perspiration-resistant make-up base [see THIS JOURNAL, **20,** 402 July, 1959)].

Bretylium Tosylate

See note on Bretylium tolysate in THIS JOURNAL, **20,** *614(Oct., 1959).*

P.G.G. of Canada has informed us that we *lysed* up the *syl* in tosylate. The item is Bretylium tosylate not tolysate.

Cantharidin—Another Source

See note on prescription including Cantharidin in THIS JOURNAL, **20,** *614(Oct., 1959).*

Another source for Cantharidin powder has been supplied by one of our readers (R.R.) as: Inland Alkaloid, Inc., Tipton, Ind.

Entero-Vioform (?)

We have a customer who will be traveling in areas where the water is untreated. He would like us to get "Autividoform" tablets to take along as an intestinal antiseptic. We cannot find the drug. Please help—M.C., Washington, D.C.

A literature search in answer to this telephoned plea could not reveal a listing of "Autividoform." It was suggested that the pharmacist should check the request. He did. His customer was positive. Phonetic association and the intended use of the product suggested a possible layman's version of Entero-Vioform (formerly Vioform) tablets. This was relayed to the pharmacist, who asked the customer if the drug could be Entero-Vioform. The pharmacist called to report that the customer appeared surprised when the question was asked, and said: "Certainly, that's what I asked for."

Kotrol—Kutrol

We have a prescription for Kotrol which is supposed to be a Parke, Davis product but is not in our catalog. Can you give us any information?—M.W., Washington, D.C.

Kotrol is the Parke, Davis trade name for the product marketed in Brazil and other South American countries. It is marketed in the United States as Kutrol Kapseals. It contains uroenterone, an extract of pregnancy urine which has been found effective in the treatment of duodenal and jejunal ulcer. The cross reference for the two trade names appears in *Unlisted Drugs,* **6,** 49(1954).

Leche de Higueron

We have a request for a product called Leche de Higueron. Is any information available?—J.A.G., New York.

The following note appears in "U.S. Dispensatory," 25th ed., 1955, p. 1691: "Under the name of *Leche de higueron* the latex of *Ficus laurifolia*—and also of *F. glabrata*—is used by the natives of South America and Panama as a vermifuge. The studies of Hall and Augustine have demonstrated (*Am. J. Hyg.,* 1929, **9,** 602) that it is a remedy of real value, especially against the Trichurus and also against the Ascaris. The active principle is a proteolytic enzyme, *ficin,* which has the remarkable power of digesting living helminths (see Andrews and Cornatzer, *J. Pharmacol.,* 1942, **74,** 129). Faust and his colleagues found it to be the drug of choice, if available, for trichuriasis (whipworm infestation) in *doses* of 60 cc. (approximately 2 ounces) of the sap. It was well tolerated and could be repeated if needed; no cathartic need be employed. The dose is the same for children and adults."

Naclex

We have a British customer who says he had a prescription for Naclex. What is it and where can it be obtained?—M.F., Washington, D.C.

Naclex is the trade name of Glaxo Labs. (British) for hydroflumethiazide. As the derivation of the name (NaCl-ex) indicates it is a diuretic which also aids salt (NaCl) excretion. Hydroflumethiazide is marketed in the U.S. as Saluron tablets and syrup by Bristol Labs.

Pituitary Extract for Insufflation

Can you give us a manufacturer of a posterior pituitary extract prepared specifically for use by insufflation.—J.G.A., Manitoba.

The posterior pituitary dosage form for insufflation is listed in "The Extra Pharmacepoeia" (Martindale), 24th ed., vol. 1, 1958, 1071 as follows: Di-Sipidin (Paines and Byrnes Ltd., England) Capsules containing 30 antidiuretic units. Glanduitrin Snuff (Gideon, Richter, England) 500 units per Gm. of powder. Piton Snuff (Organon Laboratories Ltd., London) 500 units per Gm., in lactose. Pituitary Posterior Lobe Snuff (Armour Laboratories, England) Capsules containing the equivalent of 40 units for use in Armour insufflator. We could not find a commercial U.S. listing.

Another 'FIRST'

APhA Handy DRUG REFERENCE

*All-inclusive listing of latest drugs
- All recently marketed drugs
- Research and experimental drugs
- Clinical results of old and new drugs
- Changes in dosage forms, strength and packaging
- New and nonofficial drugs

*Cross-indexing of official, generic, trade and common names

*Cumulative index for one complete year from date of first appearance

*Well illustrated

Look for it beginning in the January 1960 issue of This Journal

Progress in Medicine

Atropine Cigarettes in Asthma and Emphysema

Smoking cigarettes made of tobacco containing less than 0.06% nicotine with atropine sulfate added to permit inhalation of either 0.5 mg. or 1.45 mg. per cigarette increased the vital capacity and gave a feeling of relief in 39 patients with mild or moderate chronic asthma and emphysema, according to a report by H. Herxheimer, *Brit. Med. J.*, **2,** 167 (Aug. 15, 1959). Similar results were noted with wet 0.5% atropine aerosols. The cigarette method of administration is simpler, the dosage can be accurately controlled, and it is recommended as preferable to that of wet aerosols or stramonium cigarettes.

B.C.G. and Vole Bacillus Vaccines in Prevention of TB in Adolescents

A report on a clinical trial of B.C.G. and vole bacillus vaccines in more than 50,000 adolescents who were 14–15.5 years old when the tests were started in England in 1950 is published by the Medical Research Council, *Brit. Med. J.*, **2,** 379(Sept. 12, 1959). After statistical adjustment of the data, the tuberculosis vaccines clinical trials committee (MRC) concludes: "In assessing the benefit that would have accrued to the entire trial population from the use of vaccine for *all* those tuberculin negative on entry, the contribution to the total tuberculosis morbidity made by those initially tuberculin positive (and therefore ineligible for vaccination) had to be included. This benefit—that is, the percentage reduction in incidence of tuberculosis during the five-year period—was 59% for B.C.G. vaccine and 61% for vole bacillus vaccine." The report is discussed editorially on p. 414 of the same issue of *Brit. Med. J.*

Dartalan—Parkinsonism in Treated Mentally Defective Patients

A report on the treatment of 31 mentally defective patients with Dartalan, a phenothiazine tranquilizer, in an attempt to control their behavior disorders describes the development of signs of Parkinsonism in 15 of the patients. The reporting clinicians, W. A. Heaton-Ward, *et al.*, *Brit. Med. J.*, **2,** 407(Sept. 12, 1959), note the occurrence of oculogyric crises (movement of the eye about the anteroposterior axis) in a pair of identical twins. They state: "In this small series of cases the incidence of Parkinsonism was much greater and occurred on a much lower and less prolonged dosage of Dartalan than in any previously reported series. We consider it possibly significant, however, that, whereas all previous reports have concerned patients of normal intelligence, all our patients were mentally defective. We suggest that in the genetically determined cases of mental defect, developmental abnormalities of and, in the environmentally determined cases, damage to the basal ganglia, insufficient in itself to produce signs of Parkinsonism, may considerably lower the threshold dosage of Dartalan that can cause these signs to appear."

Griseofulvin in Acute Cattle Ringworm in Man

Systemic treatment with 1 Gm. of griseofulvin daily appeared to be the treatment of choice for acute inflammatory cattle ringworm infections of the human skin in 16 patients treated by T. Cochrane and A. Tullett, *Brit. Med. J.*, **2,** 286(Aug. 28, 1959). They note that the minimum effective dose and the optimum dose of the drug have yet to be established, and that the duration of infection does not seem to have any bearing on the response to treatment. They found: "In acute inflammatory ringworm of the beard and scalp the duration of treatment has been shortened by approximately six weeks. The pain and discomfort in the lesions and the general toxicity of the patient clear much more rapidly with griseofulvin. The duration of treatment will depend on the type of infection and tissue involved. In the present series of cases, only mild side-effects were seen in two patients. In prolonged treatment, however, as, for example, in tinea of the nails, routine blood examination is still thought advisable, although it would seem to be unnecessary when the antibiotic is given only for short periods."

Hydroflumethiazide—Clinical Study

Clinical observations indicate that hydroflumethiazide (Saluron), 3,4-dihydro - 7 - sulfamyl - 6 - trifluoromethyl - 1,2,4 - benzothiadiazine 1,1-dioxide, is a more potent orally effective diuretic than chlorothiazide; and it appears to be more potent than parenterally administered meralluride, according to R.V. Ford and J. Nickell, *Antibiotic Med. & Clin. Therapy*, **6,** 461 (1959). It produced less potassium and bicarbonate loss, with less tendency toward hypokalemic manifestations. It was repetitively effective, showed no toxicity in clinical doses (25-100 mg. daily) which were useful in hypertension and edematous states.

Lipostabil—Clinical Trial

Clinical observations on eight patients with ischemic heart disease (four with high serum cholesterol and four with wide pre-beta-lipoprotein bands) who were given 4 or 5 Lipostabil capsules daily for one month increased the second month and again the third month to the limit of tolerance (8–11 capsules daily) are reported by L.G.G. Davies and L. Murdoch, *Brit. Med. J.*, **2,** 619-(Oct. 3, 1959). Each capsule contained: alpha- and beta-lecithins of soya bean, 175 mg.; 3,4,5-polyoxyethylene-sorbitol monooleate (emulsifier), 100 mg.; and potassium theophyllinate·potassium thiocyanate (addition compound), 50 mg., and were supplied by John Ronaldson & Co., Ltd. The investigators noted no satisfactory fall in blood cholesterol. "The lipoprotein pattern, and particularly the pre-beta band, was unchanged. The clinical course of these patients was what could be expected from the natural history of this disease."

Male Fern and Mepacrine Treatments for Tapeworm in Man

Observations on 240 patients with tapeworm who were treated with male fern extraction or with mepacrine are reported by W.H. Jopling and A.W. Woodruff, *Brit. Med. J.*, **2,** 542(Sept. 26, 1959). No statistically different results were found between five different treatment regimes. The report notes: "Factors which may give rise to poor results when these regimes are used include inadequate fasting, administration of male fern in capsules instead of in a draught, and, when doses of anthelmintics of small volume are administered through a duodenal tube, failure to take into account the amount required to fill the tube before any is delivered from its distal extremity. Unfavorably false impressions of the efficacy of a treatment for tapeworms may be obtained unless patients are followed up for at least four months in cases in which the head of the worm is not recovered after treatment. Failure of treatment due to vomiting was encountered more often among those treated with mepacrine than with male fern. As vomiting in patients with *T. solium* infections may give rise to cysticercosis, treatment with mepacrine in such cases is best avoided."

Likes her coffee sweet . . . and her calories low

That's why she carries the 100-tablet bottle of Sucaryl with her when she travels. Just the idea that she's got her Sucaryl along—can have her coffee as sweet as she wants, whenever she wants, without being penalized by calories—helps make dieting lots easier. The point: Sucaryl, more and more, is becoming an important part of the daily pattern of living in (and *outside*) the home.

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"Pressure-Pak" VI-DAYLIN is boosting vitamin sales in pharmacies everywhere.

Why? Because VI-DAYLIN's delightful, new push-button container has turned vitamin-time into a real event in thousands of homes.

Sure, the lemon candy flavor always tasted wonderful to youngsters; the potent, balanced formula of eight essential vitamins has had the approval of physicians for years.

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The new "Pressure-Pak" VI-DAYLIN comes in a 12-fl.oz. size and it's the same nutritional formula that's also supplied in 3-fl.oz., 8-fl.oz. and pint bottles.

Abbott

"Pressure-Pak" VI-DAYLIN means more vitamin business for you—be sure to display this new package in your pharmacy!

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Declomycin for Suspension
Declomycin Pediatric Drops

Description: A dry, custard-flavored mixture containing Declomycin (demethylchlortetracycline; DMCT) equivalent to 900 mg. of HCl salt to make a suspension containing 75 mg./5 cc. The custard-flavored aqueous pediatric drops contain 60 mg./5 cc.

Indications: Same as for Declomycin tablets.

Administration: 600 mg. daily in 2 or 4 doses; children, 3 mg./lb. of body weight daily in divided doses.

Form Supplied: For oral suspension in 2-oz. bottles; drops in 10-cc. bottles. ℞ required.

Source: Lederle Laboratories, Pearl River, N.Y.

Durabolin Injection

Description: Each cc. of injection contains 25 mg. of nandrolone phenpropionate in a sesame oil vehicle.

Indications: To promote body tissue-building processes and reverse catabolic or tissue-depleting processes.

Administration: 1 cc. intramuscularly or subcutaneously once weekly or 2 cc. every second week. Children, 0.5 cc. weekly.

Form Supplied: 5-cc. multiple-dose vials and 1-cc. ampuls (boxes of 3). ℞ required.

Source: Organon Inc., Orange, N.J.

Otrivin HCl Nasal Solution and Sprays

Description: A 0.1% solution of Otrivin (xylometazoline) HCl for use as drops or spray and a 0.05% pediatric nasal spray solution.

Indications: Topical vasoconstrictor for symptomatic relief of nasal congestion.

Administration: Drops, 2–3 in each nostril every 3–4 hours; 1–2 sprays; pediatric, 1 spray. Repeat every 4 hours as needed.

Form Supplied: 0.1% solution in 30-ml. dropper bottles and 15-ml. plastic

squeeze bottles; 0.05% solution in 15-ml. p. s. bottles. ℞ required.

Source: Ciba Pharmaceutical Products Inc., Summit, N.J.

Povan Suspension

Description: Each cc. of strawberry flavored suspension contains pyrvinium pamoate equivalent to 10 mg. pyrvinium.

Indications: In treatment of pinworms.

Administration: Orally, 5 cc. per 22 lb. of body weight given as a single dose.

Form Supplied: 2-oz. bottles.

Source: Parke, Davis & Co., Detroit 32, Mich.

Other New Products

Chemicals, clinical trial drugs, diagnostic aids, equipment, for the retail and hospital pharmacy.

Apresoline HCl–Esidrix Tablets

Orange, Ciba-marked tablets containing in each: Apresoline (hydralazine) HCl, 25 mg., and Esidrix (hydrochlorothiazide), 15 mg. are marketed by *Ciba* for use in moderate to severe hypertension, especially if complicated by edema or impaired renal circulation; in toxemias of pregnancy; and in acute glomerulonephritis. Dosage is 1 tablet 3 times daily, adjusted to individual (maximal, 2 tablets t.i.d.). Supplied in bottles of 100. ℞ required.

Bexelettes Kessets
Bexelettes M Kessets

McKesson & Robbins has marketed Bexelettes (multivitamin tablets) containing in each: vitamin A palmitate, 5,000 u.; D, 1,000 u.; B_1 (mononitrate), 3 mg.; B_2, 3 mg.; C, 50 mg.; niacinamide, 25 mg.; B_6, 1 mg.; folic acid, 0.1 mg.; B_{12}, 2 mcg.; calcium pantothenate, 5 mg.; and E, 2 u. Bexelettes M contain in each tablet the above amounts of the same vitamins plus Fe, 25 mg.; I, 0.15 mg.; Co, 0.1 mg.; Cu, 1 mg.; Mn, 0.2 mg.; Mo, 0.2 mg.; Mg, 1 mg.; Zn, 0.5 mg.; and K, 5 mg. Dosage for each is 1 tablet (Kesset) daily. Supplied: Bexelettes in bottles of 300; Bexelettes M in bottles of 250.

Bonine—was Bonamine

Pfizer has changed its trade name for meclizine HCl from Bonamine to Bonine.

Aristocort Diacetate Syrup

A cherry flavored syrup containing 2 mg. 9α-fluoro-16α-hydroxyprednisolone (triamcinolone; Aristocort) diacetate in each 5 cc. is marketed by *Lederle* for pediatric treatment of conditions responding to triamcinolone. Dosage, initially 3–8 teaspoonfuls daily, adjusted as indicated. Supplied in 4-oz. bottles. ℞ required.

Darvo-Tran Pulvules

Pink and maroon opaque Pulvules containing in each: Darvon (dextro propoxyphene HCl), 32 mg.; Ultran (phenaglycodol), 150 mg.; and aspirin, 325 mg., are marketed by *Lilly* for relief of pain accompanied by tension and anxiety. Dosage, 1 Pulvule 3–4 times daily; for severe pain, dosage may be doubled. Supplied in bottles of 100. ℞ required.

Drocogesic No. 3 Tablets

Green, monogrammed and scored tablets containing in each: dihydrocodeine (drocode) bitartrate, 30 mg.; aluminum aspirin, 287 mg.; acetophenetidin, 150 mg.; and caffeine, 30 mg., are marketed by *Carrtone Labs.* as an analgesic. Dosage, 1–2 tablets every 3–4 hours. Supplied in bottles of 50 and 100. Requires official narcotic form.

Duo-Aqua-Drin Lozenge

Lozenges containing in each: tyrothricin, 1.5 mg.; neomycin sulfate, 5 mg.; and benzocaine, 10 mg., are mar-

keted for o-t-c sale by *McKesson & Robbins* for temporary relief of minor sore throat.

Effersyllium Powder

An effervescent bulk laxative marketed by *Stuart Co.* contains psyllium hydrocolloid (hemicellulose), sucrose, potassium bicarbonate, citric acid, and sweeteners. Supplied in 9-oz. bottles.

Femicin Tablets

Tablets containing in each: salicylamide, 225 mg.; acetophenetidin, 160 mg.; caffeine, 65 mg.; pyrilamine maleate, 15 mg.; and homatropine methylbromide, 0.5 mg., are marketed by *Thayer Labs.* for relief of symptoms of menstrual periodic distress. Supplied in three sizes for o-t-c sale.

Hycomine Syrup—Formula Change

The antitussive Hycomine syrup marketed by *Endo Labs.* now contains in each 5 cc.: phenylephrine HCl, 10 mg., in addition to Hycodan, 6.5 mg. (dihydrocodeinone bitartrate 5 mg. and homatropine methylbromide 1.5 mg.); pyrilamine maleate, 12.5 mg.; ammonium chloride, 60 mg.; and sodium citrate, 85 mg. The class B narcotic is supplied in pints and gallons.

Ku-zyme Capsules

Yellow and white capsules containing in each: amylolytic enzyme, 30 mg., and proteolytic enzyme, 6 mg., with D-sorbitol, are marketed by *Kremers-Urban* as a dietary supplement for patients with an imbalance in natural secretion of digestive enzymes and biliary-digestive dysfunction. Dosage, 1 capsule 3 times daily during meals. Supplied in bottles of 50 and 500. ℞ not required.

Medrol Tablets—New Strength

Tablets containing 16 mg. Medrol (6-methyl-delta-1-hydrocortisone) are marketed by *Upjohn* in bottles of 50. Also available are 2-mg. and 4-mg. tablets. The oral dosage must be individualized but is approximately two-thirds that of prednisolone.

Metrecal Powder

A powder stated to contain all known essential nutrients for suspension in water and taken in place of other food is marketed by *Mead Johnson* for weight control. Each 1/2-lb. can makes 4 glassfuls (daily portion) and contains 900 calories. Supplied in 1/2-lb. cans for o-t-c sale.

Mercote Vitamins

Almost tasteless forms of specially treated (Mercote) niacinamide (33.3% mix), riboflavin (25% mix), and thiamine (33.3% mix) are available to formulators of flavored vitamin products such as chewable tablets, from *Merck Chemical Division.* The Mercote vitamin powders contain U.S.P. vitamins. The vitamins are supplied in 1-Kg. to 25-Kg. quantities in 3 or 4 times the weight depending upon the 1/3 or 1/4 mix.

Mer-29 (Triparanol)

Clinical trials with Mer-29 (triparanol) a product of *Wm. S. Merrell* indicate that it lowers serum cholesterol levels when administered orally in a dose of one pearl-gray 250-mg. capsule daily. It can be represented chemically as 1-*p*-diethylaminoethoxyphenyl-1-*m*-methylphenyl-2-*p*-chlorophenyl ethanol. Reported to be well tolerated, mild nausea was noted in some patients with doses higher than 250 mg./day. The drug is not available commercially.

Nico-Met Elixir and Tablets

Knoll Pharmaceutical Co. has marketed an elixir and tablets containing in each 5 cc. or 1 tablet: Metrazol (pentylenetetrazol), 100 mg., and nicotinic acid, 50 mg., for use as a geriatherapeutic cerebral stimulant. Dosage, 5–10 cc. elixir or 1–2 tablets 3 times daily. Supplied, pints and gallons of elixir; bottles of 100 and 1,000 tablets.

Orthoxicol Syrup—New Sizes

The bronchodilating and sedative Orthoxicol syrup is now marketed by *Upjohn* in 2-oz. and 4-oz. bottles in addition to pints and gallons. Each 5 cc. contains: dihydrocodeinone bitartrate, 1.8 mg.; Orthoxine (methoxyphenamine) HCl, 17 mg.; and sodium citrate, 325 mg. Now o-t-c.

Panalba, Half-Strength Capsules

The *Upjohn Co.* has marketed capsules containing in each: Panmycin (tetracycline) phosphate complex equivalent to tetracycline HCl, 125 mg., and Albamycin (as novobiocin sodium), 62.5 mg. Dosage, based upon body weight: 30–40 lbs., 1 cap. 2 times daily; 41–60 lbs., 1 cap. 3 times daily; 61–80 lbs., 2 caps. 2 times daily or 1 cap. 4 times daily; 81–100 lbs., 2 caps. 3 times daily. Supplied in bottles of 16 and 100.

Piromen Injection

The nonprotein, nonanaphylactogenic, nitrogen containing bacterial component (Piromen) supplied as a colloidal dispersion in 10-cc. vials (4 mcg. or 10 mcg. per cc.) is now marketed by *Flint, Eaton.* It was formerly distributed by Travenol.

Pyrroxate Capsules—Formula Change

Each Pyrroxate capsule (*Upjohn*) now contains: chlorpheniramine maleate, 2 mg.; Orthoxine (methoxyphenamine) HCl, 25 mg.; acetophenetidin, 162 mg.; aspirin, 225 mg.; and caffeine, 32 mg. The chlorpheniramine maleate, 2 mg., replaces pyrrolazote, 12.5 mg., as the antihistaminic.

Singoserp–Esidrix Tablets

Scored, Ciba-marked tablets containing in each: 25 mg. Esidrix (hydrochlorothiazide) with Singoserp (syrosingopine) 0.5 mg. (No. 1) or 1 mg. (No. 2) are marketed by *Ciba* for use in mild to moderate hypertension, especially if complicated by edema, and in preeclampsia and hypertension associated with pregnancy. Dosage, depending upon individual and severity of the hypertension, one No. 1 or No. 2 tablet 3 times daily. Effect may not be noted for two weeks. Both strengths are supplied in bottles of 100. ℞ required.

Spensin–PS Tablets

Tablets containing in each: dihydrostreptomycin (as sulfate), 75 mg.; polymyxin B sulfate, 25,000 u.; activated attapulgite, 350 mg.; pectin, 45 mg.; and hydrated alumina, 70 mg., are marketed by *Ives-Cameron* for use in treatment of diarrheas. Dosage, 2 tablets initially, then 2 after each loose bowel movement (8–10 tablets daily until symptoms are controlled). Supplied in bottles of 48. ℞ required. The liquid form also is available.

Sumycin Pressules

Plastic, single-dose containers (Pressules) which deliver 1 cc. of flavored Sumycin suspension (100 mg. tetracycline HCl equivalent) are marketed by *Squibb* for pediatric use. For common pediatric infections dosage is 1 Pressule 4 times daily for 20–40-lb. child (contents squeezed directly into mouth). Supplied in packages of 12.

Synthroid Tablets

Synthroid (sodium L-thyroxine) tablets (0.05, 0.1, and 0.2 mg.) formerly marketed by Travenol are now distributed by *Flint, Eaton.*

White's A & D w/ Prednisolone Oint.

The regular vitamin A & D ointment formula of *White Labs.* is augmented with prednisolone 0.5% for its anti-inflammatory, antipruritic and anti-allergic effects. Apply locally; avoid infected areas of the skin. Supplied in 10-Gm. and 25-Gm. tubes. ℞ required.

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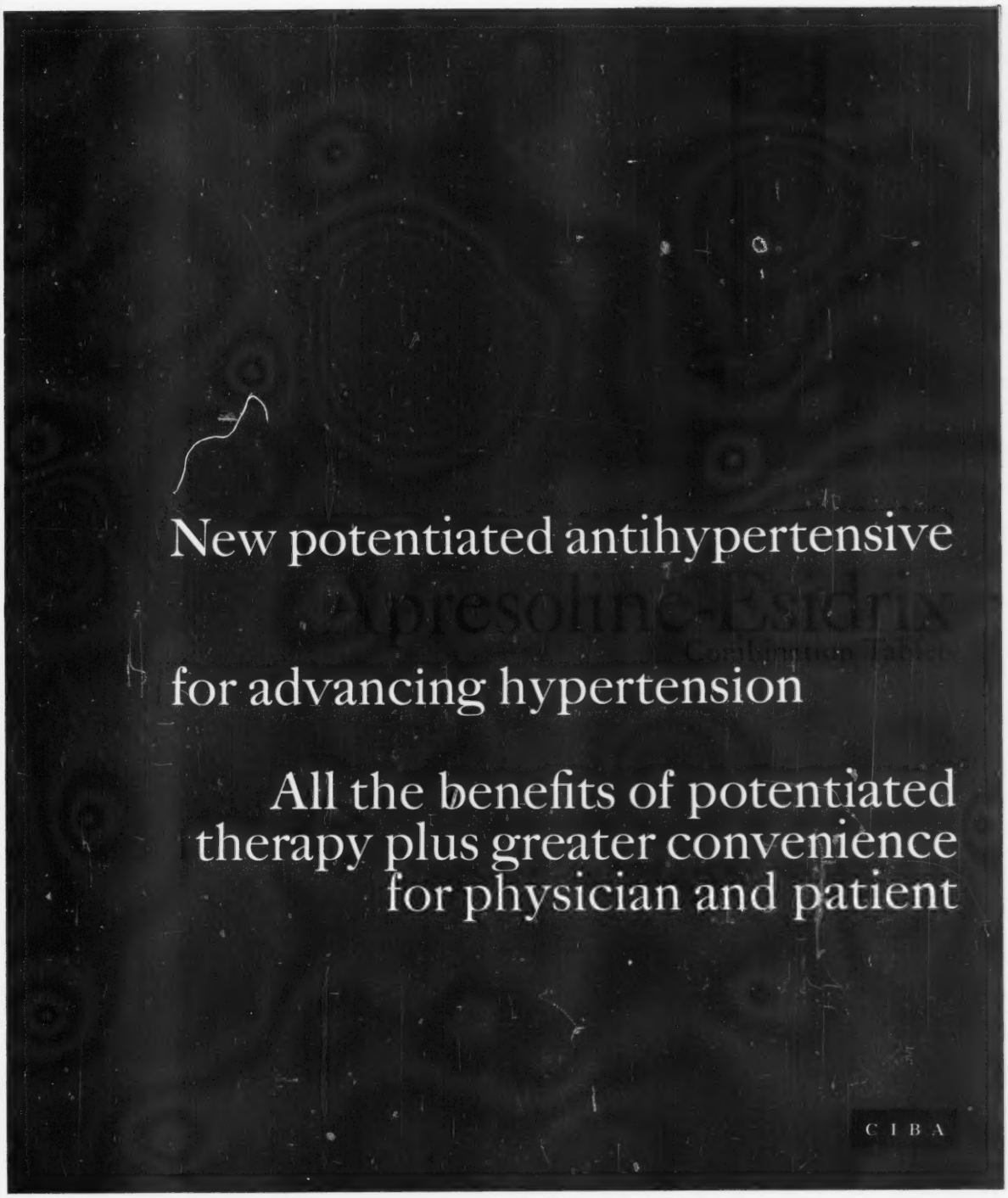

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